Figure 1

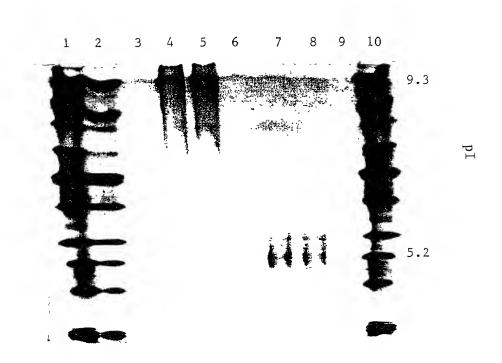


Figure 2

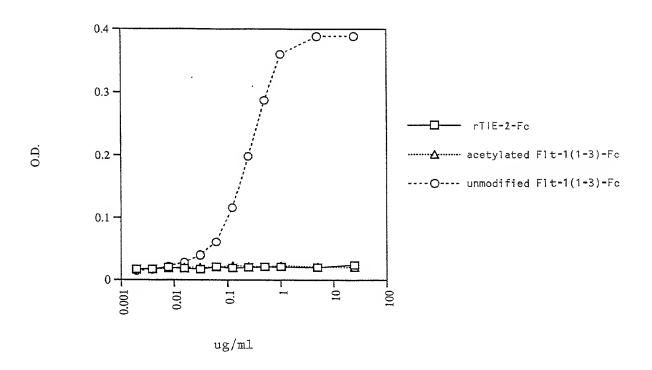


Figure 3

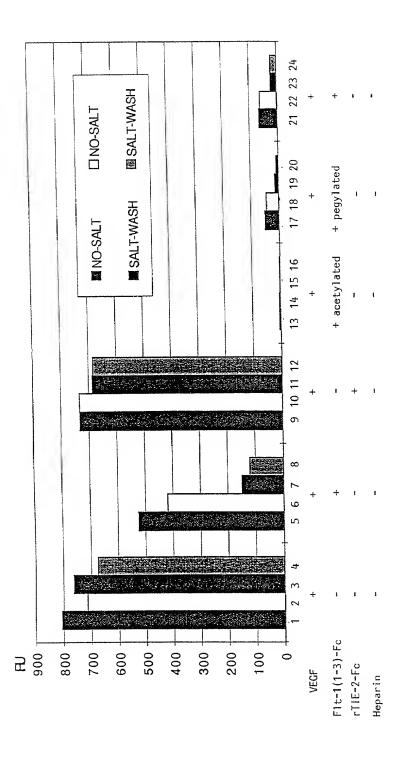


Figure 4

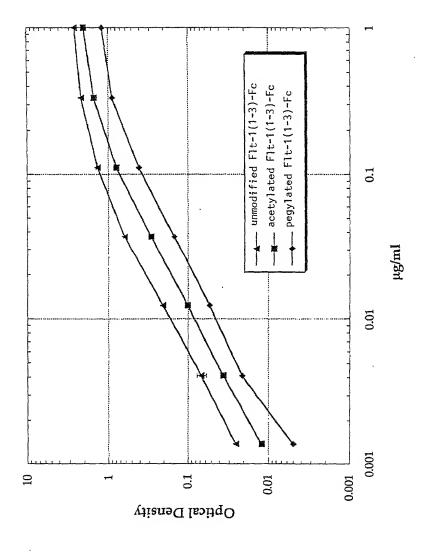


Figure 5

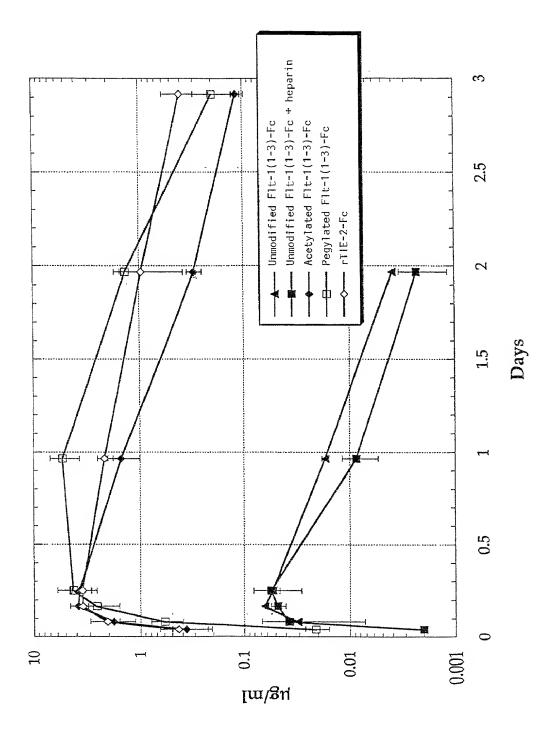


Figure 6A

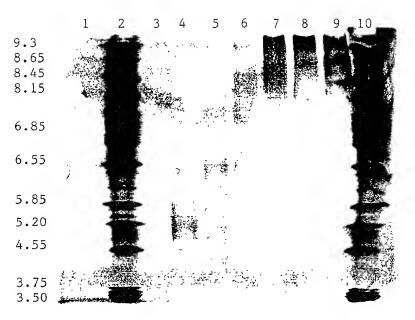


Figure 6B

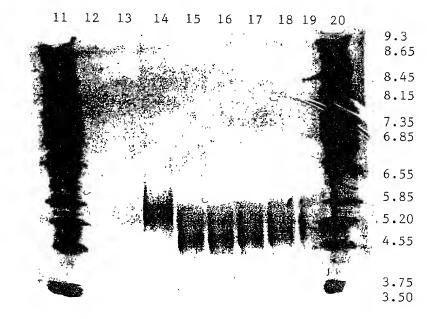
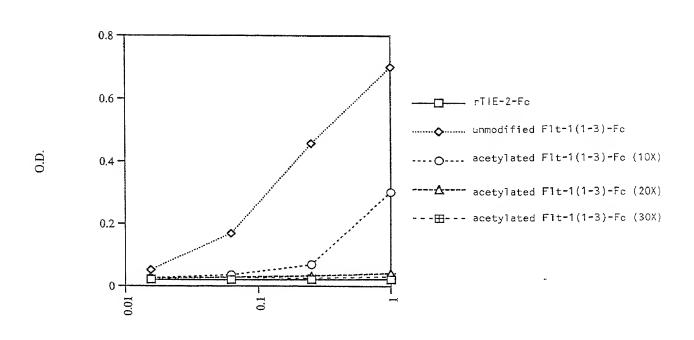
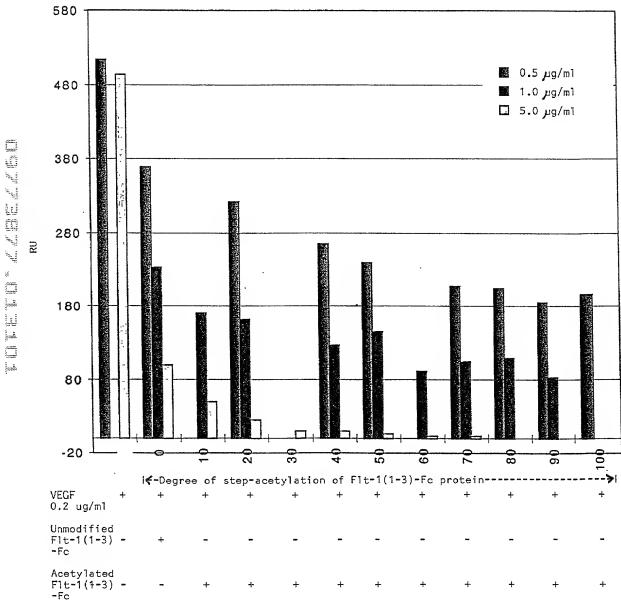


Figure 7

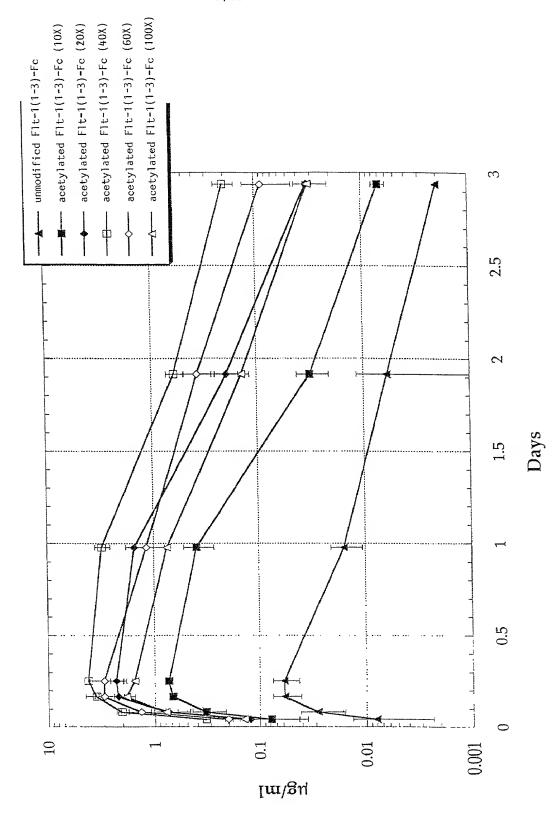


ug/ml

Figure 8



igure 9



10/65 Figure 10A

*	10 *	*	2	0 *		*	30 *		*	4	0	*		50 *		*	60 *
ATG GTC A	GC TAC	TGG (BAC A	ACC (GGG	GTC		CTG	TGC	GCG	CTG		AGC	TGT	CTG	CTT	CTC
TAC CAG T	CG ATG	ACC (erg 1	GG (CCC	CAG	GAC	GAC	ACG	CGC	GAC	GAG	TCG	ACA	GAC	GAA	GAG
Met Val S	Ser Tyr	Trp 1	R qzA	hr (G1y	Val	Leu	Leu	Cys	Ala	Leu	Leu	Ser	Cys	Leu	Leu	Leu>
	70			20			90			1.0			7	10			120
*	*	*		30 *		*	9U *		*	10	*	*	4	.10		*	120 *
ACA GGA T	CT AGT	TCA (GGT :	rca .	AAA	TTA	AAA	GAT	CCT	GAA	CTG	AGT	ATT	AAA	GGC	ACC	CAG
TGT CCT A																	
Thr Gly S	Ser Ser	Ser	Gly s	Ser	Lys	Leu	Lys	Asp	Pro	Glu	Leu	Ser	Leu	Lys	Gly	Thr	Gln>
	120		,				150			1.0			-				1.00
*	130	*	1.4	40 *		*	150		*	16	*	*	_	170 *		*	180 *
CAC ATC A	ATG CAA		GGC (ACA			CTC		TGC			GAA		GCC		
GTG TAG																	
His Ile N	Met Gln	Ala	Gly	Gln	Thr	Leu	His	Leu	Gln	Cys	Arg	Gly	Glu	Ala	Ala	His	Lys>
	100		_	0.0			010										0.40
*	190 *	*	2	00 *		*	210		*	22	20 *	*	-	230		*	240 *
TGG TCT	TTG CCT	GAA	ATG (GTG	AGT	AAG	GAA	AGC		AGG			ATA		AAA		GCC
ACC AGA																	
Trp Ser 1	Leu Pro	Glu	Met	Val	Ser	Lys	Glu	Ser	Glu	Arg	Leu	Ser	Ile	Thr	Lys	Ser	Ala>
	250		2	~ 0			070			2	20			000			200
*	250 *	*	2	60 *		*	270		*	2	80 ★	*		290 *		*	300 *
TGT GGA .	AGA AAT	' GGC	AAA	CAA	TTC			ACT		ACC			ACA		CAA		
ACA CCT																	
Cys Gly .	Arg Asr	Gly	Lys	Gln	Phe	Суз	Ser	Thr	Leu	Thr	Leu	Asn	Thr	Ala	Gln	Ala	Asn>
	310		2	20			220			,	4.0			250			3.60
*	210	*	3	20		*	330		*	3	40 ⋆	*		350 *		*	360 *
CAC ACT	GGC TTC	TAC	AGC	TGC	AAA	TAT	CTA	GCT		CCT		TCA	AAG	AAG	AAG		
GTG TGA	CCG AAC	ATG	TCG	ACG	TTT	ATA	GAT	CGA	CAT	GGA	TGA	AGT	TTC	TTC	TTC	CTT	TGT
His Thr	Gly Phe	Tyr	Ser	Cys	Lys	Tyr	Leu	Ala	Val	Pro	Thr	Ser	Lys	Lys	Lys	Glu	Thr>
	370		3	80			390			4	00			410			420
*	*	*	٠	*		*	<i>35</i> 0 ★		*	#	*	*		* *TO		*	*
GAA TCT	GCA ATY	TAT	ATA	TTT	TTA	AGI	GAT	' ACA	GGT	' AGA	CCT	TTC	GTA	GAG	ATG	TAC	AGT
CTT AGA	CGT TAG	ATA E	TAT	AAA	TAA	TCA	CTA	TGT	CCA	TCT	GGA	AAG	CAT	CTC	TAC	ATC:	TCA
Glu Ser	Ala Il	e Tyr	Ile	Phe	Ile	Ser	Asp	Thr	Gly	' Arg	Pro	Phe	Val	Glu	Met	TYX	Ser>
	430		4	140			450	1		Δ	60			470			480
*	*	*		*		*	*		*	-	*	*		*		*	*
GAA ATC																	
CTT TAG																	
Glu Ile	Pro Gl	u Ile	Ile	His	Met	Th:	Glu	ı Gly	Arc	g Glu	Leu	Va1	Il∈	Pro	Cys	Arc	y Val>
	490		4	500			510)		5	20			530			540
*	*	*		*		*	4	*	*		*	*		*		*	*
ACG TCA																	
TGC AGT																	
Thr Ser	ero As	n Ile	Thr	Val	. Thr	: Lei	ı Lys	E Lys	: Phe	e Pro) Leu	Asp	Thi	c Leu	ı Ile	e Pro	> Asp>

11/65 Figure 10B

EEO	560	570		580	590	600
550 * * *		* *	*	*	* *	* *
GGA AAA CGC ATA ATC	TGG GAC AGT	AGA AAG	GGC TTC .	ATC ATA T	CA AAT GCA AC	G TAC AAA
CCT TTT GCG TAT TAG	ACC CTG TCA	TCT TTC	CCG AAG	TAG TAT A	GT TTA CGT TG	C ATG TTT
Gly Lys Arg Ile Ile	e Tro Asp Ser	Arg Lys	Gly Phe	Ile Ile S	er Asn Ala Th	r Tyr Lys>
34 , 4 , 1 - 3			,			
610	620	630		640	650	660
	* *	* *	*	*	* *	* *
GAA ATA GGG CTT CT	G ACC TGT GAA	GCA ACA	GTC AAT	GGG CAT 1	TAT AAG AC	A AAC TAT
CTT TAT CCC GAA GAG	C TGG ACA CTT	CGT TGT	CAG TTA	CCC GTA A	AC ATA TTC TG	T TTG ATA
Glu Ile Gly Leu Le	u Thr Cys Glu	Ala Thr	Val Asn	Gly His I	eu Tyr Lys Th	r Asn Tyr>
					710	700
670	.680	690	,	700 *	710	720 * *
	* *	* *	*			
CTC ACA CAT CGA CA	A ACC AAT ACA	ATC ATA	GAT GIC	CAA ATA	BOC MOR COM CO	C CCA GIC
GAG TGT GTA GCT GT	T TGG TTA TGT	TAG TAT	TA CAG	GIT TAT	for The Dro A	ra Pro Val>
Leu Thr His Arg Gl	n Thr Asn Thr	lie lie	Asp var	GIN IIE	ser iii Pio A	tg 110 var-
720	740	750		760	770	780
730 * *	740 * *	* *	*	*	* *	* *
AAA TTA CTT AGA GG			አልጥ ጥርጥ	ACT GCT	ACC ACT CCC T	TG AAC ACG
TTT AAT GAA TCT CC	C CAI ACI CII	CAG GAG	TITA ACA	TGA CGA	TGG TGA GGG A	AC TTG TGC
Lys Leu Leu Arg Gl	ly His Thr Len	Val Leu	Asn Cvs	Thr Ala	Thr Thr Pro L	eu Asn Thr>
The neg neg wid G	ry mrs med	741 DC4				
790	800	810	•	820	830	840
* *	* *	* *	*	*	* *	* *
AGA GTT CAA ATG AG	CC TGG AGT TAC	CCT GAT	GAA AAA	AAT AAG	aga gct tcc g	TA AGG CGA
TOT CAA GIT TAC IX	GG ACC TCA ATG	GGA CTA	CTT TTT	TTA TTC	TCT CGA AGG C	AT TCC GCT
Arg Val Gln Met T	hr Trp Ser Tyr	Pro Asp	Glu Lys	Asn Lys	Arg Ala Ser V	al Arg Arg>
					200	200
850	860	870		880 *	890 * *	900
* *	* *	* *				
CGA ATT GAC CAA A	GC AAT TCC CAL	GCC AAC	J ATA TIC	TAC AGT	CAN CAN TWO T	TI GAC AAT
GCT TAA CTG GTT T Arg Ile Asp Gln S	CG TTA AGG GTA	170	a Tla Dha	Thr Ser	Val Leu Thr 1	The Asp Lvs>
Arg lle Asp Gin S	er Asn Ser His	MIG MSI	I TIE FII	a TAT Der	Vai 200 112 -	-1-
910	920	93	0	940	950	960
* *	* *		* *	*	* *	* *
ATG CAG AAC AAA G	ac aaa gga ct	r tat ac'	T TGT CG	r gta agg	AGT GGA CCA	ica tic aaa
TAC GTC TTG TTT C	TG TTT CCT GA	A ATA TG	A ACA GC	A CAT TCC	TCA CCT GGT 2	AGT AAG TTT
Met Gln Asn Lys A	Asp Lys Gly Le	u Tyr Th	r Cys Ar	g Val Arg	Ser Gly Pro	Ser Phe Lys>
_						
970	980	99		1000	1010	1020
* *	* *		* *	*	* *	* *
TCT GTT AAC ACC	ICA GTG CAT AT	A TAT GA	T AAA GC	A GGC CCG	GGC GAG CCC .	AAA TC'I' 'IG'I'
AGA CAA TTG TGG	AGT CAC GTA TA	T ATA CT	A TTT CG	T CCG GGC	CCG CTC GGG	TIT AGA AGA
Ser Val Asn Thr	Ser Val His Il	e Tyr As	p Lys Al	a GIY Pro	GIA GIA LLO	Lys Ser Cys>
	2010	305	: 0	1060	1070	1080
1030	1040	105 *)U * *		* *	* *
* * GAC AAA ACT CAC .						
CTG TTT TGA GTG	שכת דפה הרש הר פירע דפה הרש הר	KC ACG GC	T CGT GO	A CTT GAC	GAC CCC CCT	GGC AGT CAG
Asp Lys Thr His	Thr Cvs Pro Pr	to Cvs Pr	ro Ala Pr	o Glu Lei	Leu Gly Gly	Pro Ser Val>
		-				

12/65 Figure 10C

1090	1100	1110	1120	1130	1140
TTC CTC TTC CCC CC	A AAA CCC AAG	GAC ACC CT	C ATG ATC TCC C	GG ACC CCT GAG	GTC ACA
AAG GAG AAG GGG GG'	TTT GGG TTC	CTG TGG GA	G TAC TAG AGG	FCC TGG GGA CTC	CAG TGT
Phe Leu Phe Pro Pro	o Lys Pro Lys	Asp Thr Le	eu Met Ile Ser A	rg Thr Pro Glu	val Thr>
1150	1160	1170	1180	1190	1200
* *	* *	* *	* *	* *	* *
TGC GTG GTG GTG GA	C GTG AGC CAC	GAA GAC CO	CT GAG GTC AAG	TTC AAC TGG TAC	GTG GAC
ACG CAC CAC CAC CT Cys Val Val Val As	G CAC TCG GTG	CTT CTG GC	GA CTC CAG TIC	AAG TIG ACC AIG Phe Asp Tro Tur	Val Asp>
Cys vai vai vai As	p var ser mis	GIU ASP PI	eo Giu vai ilya .	2110 21011 1210 231	
1210	1220	1230	1240	1250	1260 * *
GGC GTG GAG GTG CA	T AAT GCC AAG	ACA AAG CO	CG CGG GAG GAG	CAG TAC AAC AGG	C ACG TAC
CCG CAC CTC CAC GI	A TTA CGG TTC	TGT TTC G	GC GCC CTC CTC	GTC ATG TTG TCC	TGC ATG
Gly Val Glu Val Hi	s Asn Ala Lys.	Thr Lys P	ro Arg Glu Glu	Gin Tyr Asn Sei	e Thr Tyr>
1270	1280	1290	1300 * *	1310	1320
CGT GTG GTC AGC GT	rc ctc acc gtc	CTG CAC C	AG GAC TGG CTG	AAT GGC AAG GAG	G TAC AAG
GCA CAC CAG TCG CA	AG GAG TGG CAG	GAC GTG G	TC CTG ACC GAC	TTA CCG TTC CT	C AIG TTC
Arg Val Val Ser Va	al Leu Thr Val	Leu His G	In Asp Trp Leu	Asn Gly Lys Gl	u Tyr Lys>
1330	1340	1350	1360	1370	1380
* *	* *	* *	* *	* *	* *
TGC AAG GTC TCC A	ac aaa gcc cto	CCA GCC C	CC ATC GAG AAA	ACC ATC TCC AA	A GCC AAA
ACG TTC CAG AGG T	TG TTT CGG GA	G GGT CGG G	GG TAG CTC TTT	TGG TAG AGG TI	T CGG TTT
Cys Lys Val Ser A	sn Lys Ala Lei	1 PIO ALA E	STO TIE GIG DYS	THE THE BEL BY	a mad by C
1390	1400	1410	1420	1430	1440
* *	* *	* *	* *	* *	* *
GGG CAG CCC CGA G	AA CCA CAG GIV	G TAC ACC (C ang tyge (ING CCC CCA ICC	GCC CTA CTC GA	C TGG TTC
Gly Gln Pro Arg G	alu Pro Gln Va	l Tyr Thr I	Leu Pro Pro Ser	Arg Asp Glu Le	eu Thr Lys>
2					
1450 * *	1460 * *	1470 * *	1480 * *	. 1490	1500
AAC CAG GTC AGC C					
TTG GTC CAG TCG	AC TGG ACG GA	C CAG TTT	CCG AAG ATA GGG	TOG CTG TAG CO	EG CAC CTC
Asn Gln Val Ser I	Leu Thr Cys Le	u Val Lys	Gly Phe Tyr Pro	Ser Asp Ile A	la Val Glu>
1510	1520	1530	1540	1550	1560
1510 * *	* *	* *	* *	* *	* *
TGG GAG AGC AAT (GGG CAG CCG GA	AG AAC AAC	TAC AAG ACC ACC	CCT CCC GTG C	TG GAC TCC
ACC CTC TCG TTA	CCC GTC GGC CI	C TIG TIG	ATG TTC TGG TGC	GGA GGG CAC G	AC CTG AGG
Trp Glu Ser Asn (Gly Gin Pro G	tu Asn Asn	TYP LYS THE THI	. FEO PEO VAI L	en wah pers
1570	1580	1590	1600	1610	1620
* *	* *	* *	* *		* *
GAC GGC TCC TTC	TTC CTC TAC AC	GC AAG CTC	ACC GTG GAC AAC	AGC AGG TGG C	AG CAG GGG
CTG CCG AGG AAG Asp Gly Ser Phe	AAG GAG ATG T Phe Leu Tvr S	er Lvs Leu	Thr Val Asp Lv	s Ser Arg Trp G	In Gln Gly>
wah ark ser tile	THE DOG TAT D				–

Figure 10D

1690 1700 * * *

CTC TCC CTG TCT CCG GGT AAA TGA GAG AGG GAC AGA GGC CCA TTT ACT Leu Ser Leu Ser Pro Gly Lys ***>

Figure 11

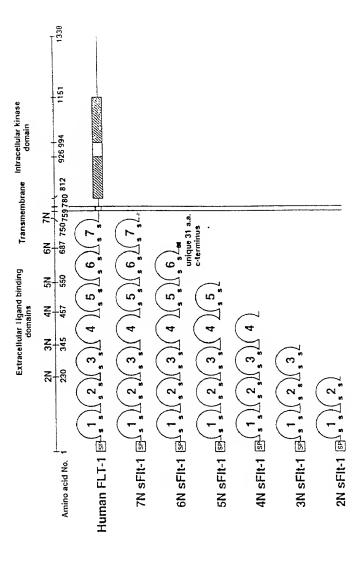
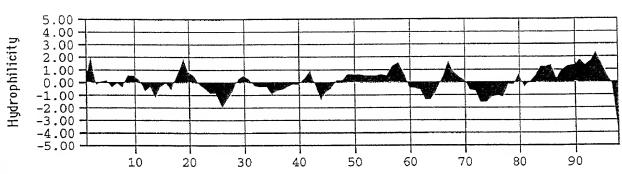
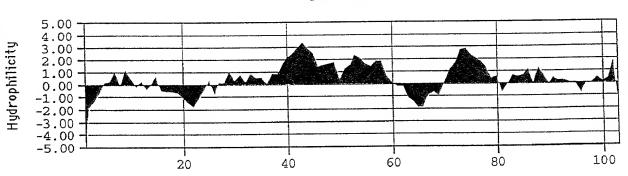


Figure 12A







1**6**/65 Figure 13A

10	20	30	40	50	60
* * *	* *	* *	* *	*	* *
ATG GTC AGC TAC TGG GAC	ACC GGG GTC	CTG CTG TGC	GCG CTG CTC AC	GC NGT CNG	CTT CTC
TAC CAG TCG ATG ACC CTG Met Val Ser Tyr Trp Asp	TGG CCC CAG	GAC GAC ACG	Ala Teu Leu S	er Cvs Leu	Leu Leu>
met val ser lyr lip Asp	Thi Giy vai	Let Let Cys .	AIG DEG DEG D	er old men	
70	80	90	100	110	120
* * *	* *	* *	* *	*	* *
ACA GGA TCT AGT TCA GGI	TCA AAA TTA	AAA GAT CCT	GAA CTG AGT T	TA AAA GGC	ACC CAG
TGT CCT AGA TCA AGT CCA	AGT TTT AAT	TTT CTA GGA	CTT GAC TCA A	AT TTT CCG	TGG GTC
Thr Gly Ser Ser Ser Gly	Ser Lys Leu	Lys Asp Pro	Glu Leu Ser L	eu Lys Gly	Thr Gln>
				4.50	1.00
130	140	150	160	170 *	180
* * * * CAC ATC ATG CAA GCA GGG	* *				
GTG TAG TAC GTT CGT CCC	CAG ACA CIG	CAT CIC CAA	ACC TOO COO	THE COT COC	GTA TTT
His Ile Met Gln Ala Gly	/Glo Tor GAC	His Leu Gln	Cvs Arg Glv G	Slu Ala Ala	His Lys>
ms ite met din Azu di	y dan ma bea		0,1 0		
190	200	210	220	230	240
* * *	* *	* *	* *	*	* *
TGG TCT TTG CCT GAA AT	G GTG AGT AAG	G GAA AGC GAA	AGG CTG AGC A	ATA ACT AAA	TCT GCC
ACC AGA AAC GGA CTT TA	C CAC TCA TTC	C CTT TCG CTT	TCC GAC TCG	rat tga ttt	AGA CGG
Trp Ser Leu Pro Glu Me	t Val Ser Lys	s Gļu Ser Glu	Arg Leu Ser	lle Thr Lys	Ser Ala>
250	260	270	280	290	300
250	260	270	* *	*	* *
TGT GGA AGA AAT GGC AA			ACC TTG AAC	aca gct caa	GCA AAC
ACA CCT TCT TTA CCG TT	T GTT AAG ACC	G TCA TGA AAT	TGG AAC TTG	TGT CGA GTI	CGT TTG
Cys Gly Arg Asn Gly Ly	s Gln Phe Cys	s Ser Thr Leu	Thr Leu Asn	Thr Ala Glr	n Ala Asn>
310	320	330	340	350	360
* * *	* *	* *	* *	*	* *
CAC ACT GGC TTC TAC AG	C TGC AAA TA	T CTA GCT GTA	CCT ACT TCA	MAG AAG AAG	GAA ACA
GTG TGA CCG AAG ATG TO His Thr Gly Phe Tyr Se	CHE LIE TY	M GAT CGA CAT	Pro Thr Ser	INS INS IN	s Glu Thr>
HIS THE GLY PHE TYL SE	er che rhe th	I bed Ard var	. IIO IIII DOL		
370	380	390	400	410	420
* * *	* *	* *	* *	*	* *
GAA TCT GCA ATC TAT AT	DA TTA TTT AT	T GAT ACA GGI	AGA CCT TTC	GTA GAG AT	G TAC AGT
CTT AGA CGT TAG ATA T	OT AAA TAA TC	CA CTA TGT CCA	A TCT GGA AAG	CAT CTC TA	C ANG TCA
Glu Ser Ala Ile Tyr I	le Phe Ile Se	er Asp Thr Gly	Arg Pro Phe	Val Glu Me	t Tyr Sel>
420	440	450	460	470	480
430 * * *	* * ##U	* *	* *	*	* *
GAA ATC CCC GAA ATT A	TA CAC ATG AC	CT GAA GGA AGO	GAG CTC GTC	ATT CCC TG	C CGG GTT
CTT TAG GGG CTT TAA T	AT GTG TAC TO	GA CTT CCT TCC	C CTC GAG CAG	TAA GGG AC	G GCC CAA
Glu Ile Pro Glu Ile I	le His Met Th	hr Glu Gly Arg	g Glu Leu Val	Ile Pro Cy	s Arg Val>
490	500	510	520 * *	530 *	540 * *
* * *	* *	* * יחיים יאל לאל ליח			
ACG TCA CCT AAC ATC A TGC AGT GGA TTG TAG T	CT GTT ACT T.	TA AAA AAG TT MUUNUU MUUN MUUN MUUN MUUN MUUN MUUN MU	A COM CIT GAC	TGA AAC TZ	G GGA CTA
Thr Ser Pro Asn Ile T	thr Val Thr I.	eu Lvs Tvs Ph	e Pro Leu Asp	Thr Leu II	le Pro Asp>
III Jei FIO ASII IIE I					-

Figure 13B

550	560	570		580	590	600
* * *		* *	*	* *	* * * * * * * * * * * * * * * * * * *	* * TAC AAA
GGA AAA CGC ATA ATC	TGG GAC AGT	AGA AAG	CCG AAG TA	AG TAT AGT	TTA CGT TGC	ATG TTT
Gly Lys Arg Ile Ile	Tro Asp Ser	Ara Lys	Gly Phe I	le Ile Ser	Asn Ala Thr	Tyr Lys>
orly ning tro tre	- 12p 110p	5 -1-	-			
610	620	630		640	650	660 * *
	*	* *	*	* *	* מסג סגת מתח	
GAA ATA GGG CTT CTC CTT TAT CCC GAA GAC	ACC TGT GAA	GCA ACA	GTC AAT GO	CC CTA AAC	ATA THE TOTAL	TTG ATA
Glu Ile Gly Leu Le	o TGG ACA CIT	Ala Thr	Val Asn G	lv His Leu	Tyr Lys Thr	Asn Tyr>
GIR TIE GIA DER DE	d lift Cha Gra	ALC III	VG2 11011 G			
670	680	690		700	710	720
	* *	* *	*	* *	*	* *
CTC ACA CAT CGA CA	A ACC AAT ACA	ATC ATA	GAT GTC C	AA ATA AGC	ACA CCA CGC	CCA GIC
GAG TGT GTA GCT GT Leu Thr His Arg Gl	T TGG TTA TGT	TAG TAT	Ash Val G	In The Ser	Thr Pro Arc	Pro Val>
Let Thr His Aig Gi	n mi Asii iir	TTG TTG	Map var o	211 220 002		,
730	740	750		760	770	780
* *	* *	* *		* *		* *
AAA TTA CTT AGA GO	C CAT ACT CTT	GTC CTC	AAT TGT A	ACT GCT ACC	ACT CCC TI	AAC ACG
TTT AAT GAA TCT CC Lys Leu Leu Arg Gl	G GTA TGA GAA	CAG GAG	TIA ACA 1	Thr Ala Thr	Thr Pro Lei	Asn Thr>
Lys Lew Lew Arg Gi	ly His THE Leo	var bed	r Mair Cya .			
790	800	810)	820	830	840
* *	* *	* *		* *		* *
AGA GTT CAA ATG AG	CC TGG AGT TAC	CCT GAT	r gaa att (GAC CAA AGO	AAT TCC CA	T GCC AAC
TCT CAA GTT TAC TO Arg Val Gln Met Ti	GG ACC TCA ATC	GGA CTA	A CTT TAA	ong Gir icc Man Gla Ser	Asn Ser Hi	s Ala Asn>
Arg val Gin Met Ti	nr Trp Ser Tyr	. PIO ASL	, G10 11C	asp cm bei		
850	860	870	0	880	890	900
* *	* *		* *		* *	* *
ATA TTC TAC AGT G	TT CTT ACT AT	r gac aa	A ATG CAG	AAC AAA GAG	C AAA GGA CT	T TAT ACT
TAT AAG ATG TCA C Ile Phe Tyr Ser V	AA GAA TGA TA	A CTG TI	T TAC GIC	Acn Ive Ac	o Iva Glv Le	a aia ida -u Tvr Thr>
lle Pne Tyr Ser V	at Leu IIII II	e Asp Dy.	p Mec OTH	1011 2,0 110,	\$ 2 ,0 0 2,	
910	920	93	0	940	950	960
* *	* *		* *		* *	* *
TGT CGT GTA AGG A	GT GGA CCA TC	A TTC AA	A TCT GTT	AAC ACC TC	A GTG CAT AT	TA TAT GAT
ACA GCA CAT TCC T Cys Arg Val Arg S	CA CCT GGT AG	T AAG TT	T AGA CAA	Asn Thr Se	r Val His I	le Tvr Asp>
Cys Arg val Arg s	ser Giy Pro Se	r rue by	5 DCI VOI	11011 1111 00		
970	980	99	90	1000	1010	1020
* *	* *	*	* *	*	* *	
AAA GCA GGC CCG C	GC GAG CCC AA	A TOT TO	T GAC AAA	ACT CAC AC	A TGC CCA C	CO ACC CCA
TTT CGT CCG GGC (CCG CTC GGG TI	T AGA AC	A CIG TIT	Thr His Th	nr Cvs Pro P	ro Cys Pro>
DAS WIG GIA LIO	ary Gra Ero r?	cy	ניב ישני בי			-
1030	1040	105		1060	1070	1080
* *	* *	*		*	* *	* *
GCA CCT GAA CTC	CTG GGG GGA CO	CG TCA G	IC TTC CTC	TTC CCC CC	LA AAA CCC A Zan anana caca an	AG GAC ACC
CGT GGA CTT GAG Ala Pro Glu Leu	GAC CCC CCT G(sc AGT CA	ad AAG GAG al Phe Leu	Phe Pro Pi	ro Lvs Pro I	ys Asp Thr>
Ata Pio Giu Leu	nen era era b	ro par A			,	

Figure 13C

1090	1100	1110	1120	1130	1140
* * * * CTC ATG ATC TCC CGG		* *	* * **********************************		
GAG TAC TAG AGG GCC	TYCE CEA CTY	CAG TGT A	ACG CAC CAC C	AC CTG CAC TCG (FTG CTT CTG
Leu Met Ile Ser Arg	Thr Pro Glu	Val Thr	Cys Val Val V	al Asp Val Ser H	His Glu Asp>
1150	1160	1170	1180	1190	1200
* * *		* *			
CCT GAG GTC AAG TTC GGA CTC CAG TTC AAC	AAC TGG TAC	GIG GAC	CCC CAC CTC C	AC GTA TTA CGG!	TIC IGT TIC
Pro Glu Val Lys Phe	APP TYPE	Val Asp	Glv Val Glu V	al His Asn Ala	Lys Thr Lys>
FIO GIU VAI DYS IIN	can inp in	,			
1210	1220	1230	1240		1260
	* *	* *	* *		* *
CCG CGG GAG GAG CA	g tac aac agc	ACG TAC	CGT GTG GTC A	GC GTC CTC ACC	CAC CAC CAC
GGC GCC CTC CTC GT	C ATG TTG TCG	TGC ATG	GCA CAC CAG	or Val Leu Thr	Val Leu His>
Pro Arg Glu Glu Gl	n Tyr Asn Ser	Inr Tyr	Arg var var	ser var ned min	vai nea min
1270	1280	1290	130	1310	1320
* *	* *	* *		* * *	* *
CAG GAC TGG CTG AA	T GGC AAG GAG	TAC AAG	TGC AAG GTC	CC AAC AAA GCC	CTC CCA GCC
GTYC CTYG ACC GAC TT	A CCG TTC CTC	ATG TTC	ACG TTC CAG .	AGG TTG TTT CGG	GAG GGT CGG
Gln Asp Trp Leu As	n Gly Lys Glu	Tyr Lys	Cys Lys Val	Ser Asn Lys Ala	Leu Pro Ala>
#220	1240	1350	136	0 1370	1380
1330	1340	* *	*	* * *	* *
CCC ATT GAG AAA AC	CC ATC TCC AA	A GCC AAA	GGG CAG CCC	CGA GAA CCA CAG	GTG TAC ACC
מכה לאה כיתר ליועה על	G TAG AGG TT	r cgg ttt	CCC GTC GGG	GCT CTT GGT GTC	CAC ATG TGG
Pro Ile Glu Lys Th	nr Ile Ser Ly	s Ala Lys	Gly Gln Pro	Arg Glu Pro Gln	Val Tyr Thr>
			1.45	n 1430	1440
1390	1400	1410		0 1430	* *
CTG CCC CCA TCC C				AGC CTG ACC TGC	CTG GTC AAA
GAC GGG GGT AGG G	CC CTA CTC GA	C TGG TTC	TTG GTC CAG	TCG GAC TGG ACG	GAC CAG TTT
Leu Pro Pro Ser A	rg Asp Glu Le	u Thr Lys	s Asn Gln Val	Ser Leu Thr Cys	: Leu Val Lys>
~					
1450	1460	* 1470) 148 * *	80 1490	1500
* * GGC TTC TAT CCC A					GAG AAC AAC
CCG AAG ATA GGG T	YG CTG TAG CO	G CAC CTY	C ACC CTC TCG	TTA CCC GTC GGC	C CTC TTG TTG
Gly Phe Tyr Pro S	Ser Asp Ile Al	la Val Gl	u Trp Glu Ser	Asn Gly Gln Pro	o Glu Asn Asn>
-					
1510	1520	153		40 1550	1560 * *
* * TAC AAG ACC ACG (* *				
TAC AAG ACC ACG (ATG TTC TGG TGC (CCT CCC GIG C	NO CONS DO	G CTG CCG AGG	AAG AAG GAG AT	G TCG TTC GAG
Tyr Lys Thr Thr	Pro Pro Val L	eu Asp Se	r Asp Gly Ser	Phe Phe Leu Ty	r Ser Lys Leu>
iji bjo im iii '		•	- -		
1570	1580	159	-	00 1610	
* *	* *	*	* *		
ACC GTG GAC AAG. TGG CAC CTG TTC	AGC AGG TGG C	AG CAG GG	SG AAC GTC TIV	. ICA IGC ICC GI I ACT ACC ACC CA	C TAC GTA CTC
TGG CAC CTG TTC Thr Val Asp Lys	TOG TOO ACC G	ate GIC CC	L TIG CAG AAC Ly Asn Val Phe	Ser Cvs Ser Va	al Met His Glu>
Thr val Asp Lys	ser and mb c	TIL GTIL GI	יות אייטיי ווער בווע		

Figure 13D

1630 1640 1650 1660 1670 * * * * * * * * * *

GCT CTG CAC AAC CAC TAC ACG CAG AAG AGC CTC TCC CTG TCT CCG GGT AAA TGA CGA GAC GTG TTG GTG ATG TGC GTC TTC TCG GAG AGG GAC AGA GGC CCA TTT ACT ALa Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys ***>

Figure 14A

		1	0			20			30			4	. O			50			60
ATG	* GTC	rac.	* ጥልጦ	* TGG	GAC	* * *	ccc	* Œ���	* ביזרים	Carc	* TYC	ഭനദ	Сш/С *	* *	AGC	ى نە: كىلى *	CTG	сил.	* CTC
		TCG																	
Met	Val	Ser	Tyr	Trp	Asp	Thr	Gly	Val	Leu	Leu	Суѕ	Ala	Leu	Leu	Ser	Сув	Leu	Leu	Leu>
		7	0			80			90			10			1	10			120
202	*	mom.	*	*	003	*	202	*	*	CITTA	×	3 m/s	*	* Cm	C 2 2	*	CCC	*	* mm
		TCT AGA																	
																			Ile>
		13	ın.		1	.40			150			7 /	50			170			180
	*	4.0	*	*	۔	*		*	*		*	Ψ,	*	*	•	*		*	*
ATA	CAC	ATG	ACT	GAA	GGA	AGG	GAG	CTC	GTC	ATT	CCC	TGC	CGG	GTT	ACG	TCA	CCT	AAC	ATC
TAT	GTG	TAC	TGA	CTT	CCT	TCC	CTC	GAG	CAG	$\mathbf{A}\mathbf{A}\mathbf{T}$	GGG	ACG	GCC	CAA	TGC	AGT	GGA	TTG	TAG
Ile	His	Met	Thr	Glu	Gly	Arg	Glu	Leu	Val	Ile	Pro	Cys	Arg	Val	Thr	Ser	Pro	Asn	Ile>
	*	19	90 *	*	2	000 *		*	210		*	2	20	*	:	230		*	240
ACT		ACT	TTA	AAA	AAG		CCA			ACT	TTG	ATC	CCT	GAT	GGA	AAA	CGC	ATA	ATC
TGA	CAA	TGA	AAT	TTT	TTC	AAA	GGT	GAA	CTG	TGA	AAC	TAG	GGA	CTA	CCT	TTT	GCG	TAT	TAG
Thr	Val	Thr	Leu	Lys	Lys	Phe	Pro	Leu	Asp	Thr	Leu	Ile	Pro	Asp	Gly	Lys	Arg	Ile	Ile>
		2	50		:	260			270			2	80			290			300
	*		*	*		*		*	*		*		*	*		*		*	*
		AGT																	
		TCA																	
Trp	Asp	Ser	Arg	гЛs	GIĀ	Pne	TTE	TTE	Ser	ASN	Ala	unr	ıyr	гўs	Glu	тте	GTĀ	Leu	Leu>
	*	3	10 *	*		320		*	330 *		*	3	40 *	*		350		*	360 *
ACC		GAA			GTC		GGG			TAT		ACA					CAT		
																			GTT
Thr	Cys	Glu	Ala	Thr	Val	Asn	Gly	His	Leu	Tyr	Lys	Thr	Asn	Tyr	Leu	Thr	His	Arg	Gln>
	*	3	70			380			390			4	.00			410			420
ACC		מים י	አ ጉጥር	בית בי	. СЪТ	. C±u∧ *	ממי	* ልጥል	* ጉርጎል .		~ ~	CGC	* ' (^^2	* حسر			CTY	. א⊂ס גיי	. GGC
																			CCG
Thr	Asn	Thr	Ile	Ile	qzA :	Val	Gln	Ile	. Ser	Thr	Pro	Arg	Pro	Val	. Lys	Leu	Leu	Arg	Gly>
		4	30			440			450	ı		4	.60			470			480
	*		*	*		*		*	*		*		*	*		*		*	*
																			ACC
																			TGG
UTE	> T11T	. net	r vari	. net	, ASI	. CAS	11)1	. Alc	1 111.	1111	LI C	, ner	. ASI	ı lili	. Aug	y val	. GLI	. Met	Thr>
	*	4	90 *	,	k	500 *		*	510 *		*	5	520 *	,		530 *		*	540 *
TG	AG	TAC	CCI	GA1	GAA	ATT	GAC	CAA	A AGC	raa :	TCC	CAT	GCC	: AAC	TA :	TTC	TAC	: AGT	GTT
																			A CAA
Tr	Se	г Туг	Pro	Ası) Gli	ı Ile	Asp	Gli	n Ser	Asr	ı Sei	His	s Ala	a Asr	111e	e Phe	e Tyr	Sei	· Val>

Figure 14B

	550)		56	0			570				580)		5	90			600	
*	,	ĸ	*		*		*	*		*			*	*		*		*		*
CTT ACT	ATT (GAC A	AAA	ATG C	AG A	AAC .	AAA	GAC	AAA	GG	A C	TT !	TAT	ACT	TGT	CGT	GTA Cam	AGG	AG.	<u>+</u> ′
GAA TGA Leu Thr	TAA	CTG '	rtr :	rac c	TC '	rig	TTT	CIG	TYPT	CC	er G. Sert.	AA A	ATA Tur	Thr	ACA Cvs	Ara	Val	Ara	Se	r>
Leu Thr	ile A	Asp 1	rās i	Met (Jili.	ASII	пЪр	ASP	пуs	Gı	.y 11	cu	13-		0,0	3				
	61	0		62	20			630				64	0		ϵ	550			66	
*		*	*		*		*	*		+			*	*		*		*		*
GGA CCA	TCA	TTC .	AAA	TCT (GTT	AAC	ACC	TCA	GTG	CZ	A TA	ATA	TAT	GAT	AAA	GCA	GGC	CCG	GG	iC 'G
CCT GGT Gly Pro	AGT	AAG	TTT	AGA (CAA	TTG	TGG	AGT	CAC	: G:	l'A'I	AT AT	Mara Mara	Agn	TAT	Ala	Glv	Pro	Gl	.y>
GIA bro	Ser	Pne	гĀг	ser	val	ASII	1111	Ser	٧٤٦			-10	-1-	1101						-
	67	0		6	80			690				70	0		•	710			72	
*		*	*		*		*	*			*		*	*	~~-	*	~~ ~	*	~	*
GAG CCC	AAA	TCT	TGT	GAC	AAA	ACT	CAC	ACA	TGO	2 0	CA (CCG	TGC	CCA	GCA	CCI	GAA	CIC		7C
CTC GGG Glu Pro	TTT	AGA	ACA	CTG	TTT	TGA	GIG	TGT	ACC	ښانئ ⊂1 د	en i	BYO.	CVS	Pro	Ala	Pro	Glu	Let	Le	eu>
Glu Pro	ьуs	ser	Суѕ	ASP	гĀг	1111	птэ	1111	Cy.	<i>.</i>			0,10							
	73	30		7	40			750)			76	50			770			7	80
*		*	*		*		*	4			*		*	*		*		*	. ~	*
GGG GGA	CCG	TCA	GTC	TTC	CTC	TTC	CCC	CCA	AA A	A C	CC I	AAG	GAC	ACC	CTC	MAC	ATC MAC	ייייני ארני מאור ב	. O	GC GC
CCC CCT	GGC	AGT	CAG	AAG	GAG	AAG	GGG	GGI	r Tar	T G	166 170	INS	Asp	Thr	Lev	Met	: Ile	Se:	- A	rg>
GIA GIA	Pro	sei	Val	PHE	neu	F.16	FIC	,	J LLY			-10								
	7	90		8	300			810)			8	20			830			8	40
*		*	*		*		*		*		*		*	*		*	- C/F/	*	~ m	*
ACC CCT	GAG	GTC	ACA	TGC	GTG	GTG	GTC	GA	CGI	G Z	YGC	CAC	GAA	L GAC		L GAC	G'IV	LAND T	5 1 C A	AG
TGG GGA	A CTC	CAG	TGT	ACG	CAC	CAC	VAC	l Ac	o Va	ו ב	er Ser	His	Gli	. Cro ı Ast	Pro	o Gli	ı Va	l Ly	s I	he>
TRI PIC) GIU	. val	1111	Cys	Val	V 04.1	. ۷۵.		, ,					•						
	8	50			860			87				8	80			890		-1-	5	00e *
*		*	*		*		*		*		*	3.3.0	*	*		*	ים כיז	* ~ ~ ~ ~ ~	G (
AAC TGC	G TAC	GTG	GAC	: GGC	GTG	GAC	GIY	G CA	D AA	DD (300 700	THY	· LACE	ነ <i>ብ</i> ብር	; CC(g GC	C CI	C CI	 C	GTC
Asn Tr	J AIN n Thar	· Val	Asr	Glv	· Val	i Gli	ı Va	l Hi	s As	sn i	Ala	Lys	Th	r Lys	s Pr	o Ar	g Gl	u Gl	u	Gln>
12211 121	P -J-			2																
	9	910			920			93			*	9	40 *		*	950 *		*		960 *
TAC AA	~ 3.00	*	, m.s.		* . ~~~	~ ~m	* ~ ~~	~ ~n	*	بـكبلا		CTY					C TO		G.	
TAC AA	C AGA	I ACC	ארר ב אינג י	CG1	CAC	CA	C AG G TC	G CZ	AG G	AG	TGG	CAC	GA	C GTY	G GT	C CI	G AC	C G	4C	ATT
Tyr As	n Se:	r Thi	r Tyj	. Arg	va:	l Va	l Se	r Va	al L	eu	Thr	Va:	l Le	u Hi	s Gl	n As	p Ti	p Le	eu	Asn>
-			_																	.020
		970			980				90 *		*	1	000		*	1010	:	*		.020
* GGC AA	יכי כיזי	א מידי ב <i>י</i>		* ~ ጥሩ	* && ~	ය යා	* YC: TYC			AA		CT								ACC
CCG TIT	~ ~~	~ AT	ር ጥጥ	CAC	արդրար	C CA	G AG	G T	IG T	TT	CGG	GA	G GC	T CG	GGC	G TI	YG C	IC T	ΓT	TGG
Gly Ly	rs Gl	u Ty	r Ly	s Cy	s Ly	s Va	l Se	er A	sn L	ys	Ala	Le	u Pr	o Al	a Pi	ro II	Le G	lu L	ys	Thr>
																1070				1080
,		030		*	1040 *		*	10	50 *		*	1	060		*	TO 1		*	•	*
מיזירי יוזיר	מג ״ר	A GC	C AA	a GG	G CA	G CC	c	ga G	AA C	CA	CAG	GI	G TA	AC AC	c c'	rg c	cc c	CA T	CC	CGG
TAG AC	द्भ गग	YT CO	G TT	T CC	C GI	C GC	G G	CT C	TT C	GT:	GTC	CA	C A	rg tr	G G	AC G	GG G	GT A	GG	GCC
Ile Se	er Ly	s Al	а Гу	s Gl	y Gl	n Pi	ro A	rg G	lu I	Pro	Glr	ı Va	1 Ty	yr Th	ır L	eu P	ro P	ro S	er	Arg>

Figure 14C

		109	90		11	.00		1	110			112	20		11	.30		1	140
	*		*	*		*		*	*		*		*	*		*		*	*
GAT	GAG	CTG	ACC	AAG	AAC	CAG	GTC	AGC	CTG	ACC	TGC	CTG	GTC	AAA	GGC	TTC	TAT	CCC	AGC
CTA	CTC	GAC	TGG	TTC	TTG	GTC	CAG	TCG	GAC	TGG	ACG	GAC	CAG	$\mathrm{T}\mathrm{T}\mathrm{T}$	CCG	AAG	ATA	GGG	TCG
Asp	Glu	Leu	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser>
		115			1.3								30			L90		_	200
	*										*							*	*
											CCG								
											GGC								
Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	G1n	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro>
	*	12:	10 *		13				1230				40			250			L260
000		~~~			~~~				*		*				200		~1.0	*	
											TAC								
											ATG								
PLO	val	Leu	Asp	Ser	ASD	GTĀ	ser	Pne	Pne	Leu	TAL	Ser	гЛг	ьeu	Thr	Väl	Asp	ьуs	Ser>
		12	70		1	280			1200			12	00		1	210			1320
	*	14	*	*	1.				*		*				1.				±
AGG	TYC	CAG									GTG				CCT	CTG	CAC	מבר	CAC
											CAC								
																			His>
				2															
		13	30		1	340			1350										
	*		*	*		*		*	*		*								
TAC	ACG	CAG	AAG	AGC	CTC	TCC	CTG	TCT	CCG	GGT	AAA	TGA							
ATG	TGC	GTC	TTC	TCG	GAG	AGG	GAC	AGA	GGC	CCA	TTT	ACT							
Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Pro	Gly	Lys	***	>						

Figure 15A

	*	1	.0	*		20		*	30		*	4	: O *	*		50		*	60 *
ATG	GTC	AGC		TGG	GAC		GGG	GTC		CTG	TGC	GCG	CTG	CTC	AGC	TGT	CTG	CTT	CTC
TAC	CAG	TCG	ATG	ACC	CTG	TGG	CCC	CAG	GAC	GAC	ACG	CGC	GAC	GAG	TCG	ACA	GAC	GAA	GAG
Met	Val	Ser	Tyr	Trp	Asp	Thr	GJA	Val	Leu	Leu	Суѕ	Ala	Leu	Leu	Ser	Cys	Leu	Leu	Leu>
	*	7	70 *	*		80		*	90		*	10)O *	*	3	.10 *		*	120
ACA	GGA	TCT	AGT	TCC	GGA	GGT	AGA	CCT	TTC	GTA	GAG	ATG	TAC	AGT	GAA	ATC	CCC	GAA	TTA
					CCT														
Thr	Gly	Ser	Ser	Ser	Gly	Gly	Arg	Pro	Phe	Val	Glu	Met	Tyr	Ser	Glu	Ile	Pro	Glu	Ile>
	*	13	30	*	1	.40 *		*	150		*	1.6	50 *	*	3	L70 *		*	180
ATA	CAC	ATG	ACT	GAA	GGA	AGG	GAG	CTC	GTC	TTA	CCC	TGC	CGG	GTT	ACG	TCA	CCT	AAC	ATC
					CCT														
Ile	His	Met	Thr	Glu	Gly	Arg	Glu	Leu	Val	Ile	Pro	Cys	Arg	Val	Thr	Ser	Pro	Asn	Ile>
		1	90		•	200			210			2.	20		:	230			240
	*	-	*	*		*		*	*		*		*	*	•	*		*	*
ACT	GTT	ACT	TTA	AAA	AAG	TTT	CCA	CTT	GAC	ACT	TTG	ATC	CCT	GAT	GGA	AAA	CGC	ATA	ATC
					TTC														
'I'nr	Val	Thr	Leu	Lys	Lys	Phe	Pro	Leu	Asp	Thr	Leu	Ile	Pro	Asp	GTA	Lys	Arg	Ile	Ile>
		2	50		:	260	•		270			2	80		:	290			300
	*		*	*		*		*	*		*		*	*		*		*	*
					GGC														
					CCG														GAC Leu>
115	ىرىدە	Der	AL 9	пуs	Giy	F 11C		110	Der	D-311	nia	111	+ Y +	БŽЗ	014	110	GLY	neu	Ded,
		3	10			320			330			3	40			350			360
3.00	*		*	*		*	. ~~~	*	*		*	. ~.	*	*	-	*	~~ m	*	*
					GTC CAG														
																			Gln>
	-						-			_	•			-				_	
	*	3	70	*		380		*	390		*	4	00 +	4		410		*	420
ACC		' ACA			GAT		CAA					CGC		GTC	AAA		Curr		GGC
					CTA														
Thr	Asr	1 Thr	Tle	: Ile	Asp	Val	Gln	Ile	Ser	Thr	Pro	Arg	Pro	Val	Lys	Leu	. Leu	Arg	Gly>
		,	120			440			450			4	c0			470			4.00
	*	4	¥	+	ŧ	440		*	450		*	4	60 *	*		470		*	480 *
CAT	AC	r cri	GTO	CIC	raa :	TGT	r ACI	GCI	. ACC	ACI	. 666	TTG	AAC	ACG	AGA	GTT	CAA	ATG	ACC
																			TGG
His	Thi	r Lei	ı Val	Let	ı Asr	Cys	s Thr	Ala	i Thi	Thr	Pro	Lev	Asr	Thr	Arg	Val	. Gln	Met	Thr>
	*	4	190 *	,	*	500 *		*	510		*	5	20	,		530		*	540 *
TGC	3 AG	AT TA		r gar	r gaz	AA A	A AAT	AAC	G AG	GC:	r TCC	GTA	AGG	G CG#	A CGA	ATT	GAC	CAA	AGC
																			TCG
Tr	Se:	r Ty:	r Pro	o Asi	o Gli	ı Ly:	s Asr	ı Lys	s Arg	, Ala	a Ser	· Val	Arg	y Arg	g Arc	; Ile	e Asr	Gln	Ser>

Figure 15B

		55	0		5	60			570			58	30		5	90			600
	*		*	*	_	*		*	*		*		*	*		*		*	*
													GAC						
													CTG						
ASII	Ser	UIS	Ala	ASII	TIE	PHE	TAT	ser	vai	neu	1117	TTE	Asp	пХр	nec	GIA	ASII	ny s	vaħ-
		61	10		6	20			630			64	10		6	550			660
	*		*	*		*		*	*		*		*	*		*		*	*
													TTC						TCA
													AAG						AGT Ser>
БУБ	GIY	nea	IYL	12.4	Cys	AL G	var	AL G	Der	GLY	110	Der	1110	nys	DCI	Val	ABII	1111	DCIP
		61	70		€	80			690			70	00			710			720
~	*		*	*		*		*	*	~-~	*		*	*	~~~	*		*	*
													TCT AGA						
																			Thr>
			-	•	2		_		-			-		-	-	-			
		7	30		•	740			750		*	7	60 *			770 *		*	780 *
ū √ Ξ∕~	~ ~	ccc		رص *	CCA	*	CNN	с шс	Cux:	ccc		ccc	* TCA	Cπ∕-	بالملتان		ילאינארי		
													AGT						
																			Pro>
		_																	
	*	7	90	*		800 *		*	810		*	8	20	*		830		*	840 *
AAA		AAG			CTC		ATC			ACC		GAG	GTC		TGC		GTG		
													CAG						
Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp>
		c	50			860			870			Ω	80			890			900
	*	C	*	*		*		*	*		*	O	*	*		*		*	*
GTG	AGC	CAC	GAA	GAC	CCT	GAG	GTC	AAG	TTC	AAC	TGG	TAC	GTG	GAC	GGC	GTG	GAG	GTG	CAT
																			GTA
Val	Ser	Hls	: Glu	. Asp	Pro	GIu	. Val	Lys	Phe	Asn	Trp	Tyr	· Val	. Asp	GLY	Val	Glu	. Val	His>
		5	910			920			930			9	940			950			960
	*		*	*		*		*	*		*		*	*		*		*	*
																			GTC
																			CAG Val>
							, 0			2 -						,			
		9	970			980			990	1		10	000		3	.010			1020
Cm/C	*	- CIIV	*	* (~~	י מאר	* 	י תעייר	* • েলং	ד חליל ב	ء (تارير :	* ን አለር ፣	2 (C)N(* ኋ መአረ	* * * * * * *	י קעייר	* * * * * * * * * * * * * * * * * * * *	י ריווער	× 11777	* ~ ~ ~ ~
																			D AAC F TTG
																			Asn>
	*	1	030	,	<u>1</u>	L040 *		*	1050		*	10	060 *	,		L070 *		*	1080
AAA		CT					GAC					CAA					G CCC		A GAA
																			r ctt
																			g Glu>

25/65 Figure 15C

		109	90		11	.00		1	110			112	0		11	.30		1	140
	*		*	*		*		*	*		*		*	*		*		*	*
CCA	CAG	GTG	TAC	ACC	CTG	CCC	CCA	TCC	CGG	GAT	GAG	CTG	ACC	AAG	AAC	CAG	GTC	AGC	CTG
GGT	GTC	CAC	ATG	TGG	GAC	GGG	GGT	AGG	GCC	CTA	CTC	GAC	TGG	TTC	TIG	GTC	CAG	TCG	GAC
Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Asp	Glu	Leu	Thr	Lys	Asn	Gln	Val	Ser	Leu>
		115	50		11				1170							L90			.200
	*		*	*		*		*	*		*		*	*		*		*	*
					GGC														
					CCG														
Thr	Cys	Leu	Va1	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	G1u	Ser	Asn	GJy>
		12:				220			1230				10			250			.260
	*			*		*			*		*							*	
					TAC														
					ATG														
Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe>
																24.0			
	*	12	/U *	*		280 *			1290 *		4	1.5	00		1.	310		-	L320 *
ama.		* 00					~-~										mm-c		
					ACC														
					TGG														
ueu	TYL	SEL	туs	Leu	TILL	val	ASD	пур	SET	ALG	пъ	GIH	GTII	GTĀ	ADII	var	File	Ser	Cys>
		13	3.0		7	340			1350			12	60		1	370			1380
	*	10	*	*	_				*		*	1.5	*						*
יזעיר	· CTY	באדע	דבר)	CAC	GCT.	CTC	CAC	AAC	CAC	TAC	ACG	CAG	AAG	AGC	СТС	ጥርር	CTC	ጥረጥ	CCG
																			GGC
																			Pro>
										-2-						~ ~ ~			
	*																		
GG1	' AAA	TGA																	
	י יוואדויות																		

GGT AAA TGA CCA TTT ACT Gly Lys ***>

Figure 16A

		נ	.0			20			30			4	.0			50			60
ATG	* GTC	AGC:	* TAC	* TGG	GAC	* ACC	GGG	* GTC	* CTG	CTG	* TGC	GCG	* CTG	CTC	AGC	* TGT	CTG	* CTT	* CTC
TAC	CAG	TCG	ATG	ACC	CTG	TGG	CCC	CAG	GAC	GAC	ACG	CGC	GAC	GAG	TCG	ACA	GAC	GAA	GAG
Met	Val	Ser	Tyr	Trp	Asp	Thr	Gly	Val	Leu	Leu	Cys	Ala	Leu	Leu	Ser	Cys	Leu	Leu	Leu>
			70			80			90			10	00		1	10			120
	*		*	*		*		*	*		*		*	*		*		*	*
														AGT					
														TCA					GTC Gln>
TITE	GTĀ	ser	ser	Ser	GTĀ	Ser	пĀг	Leu	пуs	АБР	PLO	GIU	neu	Der	nea	пуъ	GLY	1111	GIII>
	*	1.	30	*	1	. 4 0		*	150		*	16	50 *	*	:	170		*	180
CAC		ATG			GGC		ACA			CTC		TGC		GGG	GAA		GCC	CAT	AAA
GTG	TAG	TAC	GTT	CGT	CCG	GTC	TGT	GAC	GTA	GAG	GTT	ACG	TCC	CCC	CTT	CGT	CGG	GTA	TTT
His	Ile	Met	Gln	Ala	Gly	Gln	Thr	Leu	His	Leu	Gln	Cys	Arg	Gly	Glu	Ala	Ala	His	Lys>
		1	90		2	200			210			2	20			230			240
maa	*	mma	*	*	3 m/s	*	3 Cm	*	*	700	* ~~~~	7.00	* ~~~	* AGC	אנטא	ارس. *	**	ιπ∕_π. *	* CCC
														TCG					
																			Ala>
		_				250			070			^	00			200			300
	*	2	50	*		260 *		*	270		*	4	80 *	*		290 *		*	*
TGT	GGA	AGA	LAA	GGC	AAA	CAA	TTC	TGC	AGT	ACT	ATT	ACC	TTG	AAC	ACA	GCT	CAA	GCA	AAC
																			TTG
Cys	Gly	Arg	Asn	Gly	Lys	Gln	Phe	Cys	Ser	Thr	Leu	Thr	Lev	ı Asn	Thr	Ala	. Gln	Ala	Asn>
		3	10			320			330			3	40			350			360
	*		*	*		*		*	*		*		*	*		*		*	*
																			ACA TGT
																			Thr>
				1		-2			_						_	-	-		
	*		370 *	4		380		*	390		*	4	* *	*		410		*	420 *
GAA		r GCI					. ATI					r AGA					YEA E		AGT
CTI	AGA	A CG	r TAC	G AT	LAT A	' AAA	AT A	TCI	A CTA	A TGT	r cca	A TCI	r GG2	A AAC	CAT	CTC	TAC	OTA :	TCA.
Gli	ı Sei	r Ala	a Ile	e Tyı	: Ile	Phe	≥ Ile	e Sei	Asp	Thi	c Gly	7 Arg	g Pro) Phe	e Val	L Gli	ı Met	Туг	Ser>
			430			440			450)		4	160			470			480
	*		*		+	*		*	4		*		*		k	*		*	*
																			GTT
																			CCAA g Val>
02.			0 01.	u 11.					. 0=	. 0	, .—:	5 02.						,	, ,
	490					500			510			!	520 *		L	530 *		*	540 *
200	* ~m~	ъ cc	מבית. *	ሮ አሙ	~ <i>^</i>	* ייים יי	ייס גיד	יידאידו יך *		* A A A	امان ات *	ד ככ			* " AC'		ር ልጥ		r gat
																			A CTA
																			o Asp>

Figure 16B

		5	50			5	60			570			*		580		*	5	90		*	6	00 *
GGA	* ~ ~ ~ ~	CCC	*	איר 7	/ u/\ : *	בעמד	~ G2C	۳۵۳	*			GC '		ΑT	YC A	' AT	TCA	AAT	GCA	ACG	TA	C A	AA
C	لمشه	GCC	7 T	AT 1	rag .	ACC	CTG	TCA	TCT	TT	C C	CG 3	AAG	TA	G I	TAT.	AGT	TTA	CGT	TGC	AΤ	G T	$\Gamma_{a}\Gamma_{c}$
Gly	Lys	Arg	gI	le :	[le	Trp	Asp	Ser	Arg	Ly	s G	ly :	Phe	IJ	.e 1	[le	Ser	Asn	Ala	Thr	Ту	r L	ys>
										ć 2.	^				CAC	٦.		4	550			6	60
	*	(610 *		*	6	520 *		*	63	∪ *		*		640		*	,	*		*	Ü	*
GAA	ATA	GG	G C	TT (CTG	ACC	TGT	GAA	GCA	. AC	A G	TC	TAA	G	GG (TAC	TTG	TAT	AAG	ACA	AA	C T	AT
CTT	TAT	CC	C G	AA (GAC	TGG	ACA	CTT	CGT	TG	T C	AG	ATT	_C(CC (GTA	AAC	ATA	TTC	TGI	TT	G A	TA
Glu	Ile	G1;	уL	eu :	Leu	Thr	Cys	Glu	Ala	Th	r V	al	Asn	G.	ly I	His	Leu	Tyr	Lys	Thr	· As	n T	yr>
			C77 C	,			680			69	10				70	n			710			7	20
	*		670 *	÷	*		*		*		*		ж			*	*		*		*		*
CTC	AC/	A CA	T C	CGA	CAA	ACC	TAA	ACA	ATC	ra :	'A C	TAE	GTC	. C	AA .	ATA	AGC	ACA	CCA	CGC	CC	A C	TC
GAG	יועליני	r GT	'A C	3CT	GTT	TGG	TTA	TGT	TAC	TA	T/	ΔT	CAC	G	${ m TT}$	TAT	TCG	TGT	GGI	GCC	G GC	T	AG
Leu	Th	r Hi	s ?	Arg	Gln	Thr	Asn	Thr	Ile	∋ Il	e P	Asp	Va.	. G	ln	lle	ser	'I'nr	Pro	Arg	j Pi	:O \	/d1>
			730	n			740			75	50				76	0			770				780
	*			*	*		*		*		*		*			*	*		*		*		*
AAA	TT	A CI	et 1	AGA	GGC	CAT	ACI	CTI	GIY	C C:	IC 1	TAA	TG	r A	CT	GCT	ACC	ACT	. CCC	TT	G A	AC A	ACG
TTT	AA	T G	' A.	TCT	CCG	GTA	TGA Thr	GAZ	CA	G G2	AG '	TTA	AC	A I	YGA Thr	CGA Ala	TGG Thr	TGF	. GG - Pro	a AAI a Le	u A	sn '	IGC Thr>
Lys	Lе	u Le	∋u .	Arg	GIĀ	nis	1111	. ner	ı va	T 77	eu .	non	Cy.										
			79	0			800			8	10				82				830				840
	*			*	*		*		*		*		*			*	*		*	- OF	*		*
AGA	GI	T C	AA mm	ATG	ACC	TGO	AG:	ATT T	2 CC	TG.	AT :	GAA	AA. TPTP	A. Æ ጥ ጣ	νπα ¥ΑΩ	TITO	ייייייני ארייייי	CG	A AG	o Gi G CA	A A T T	CC.	GCT
Arc	. CA	l G	ln	Met	Thr	Tr	Se:	Ty	r Pr	o A	sp	Glu	Ly	s A	Asn	Lys	Asr	Ala	a Se	r Va	1 A	rg	Arg>
						_																	
			85	* *	4		860 *		*	8	70 *		*		8	80 *	,	,	890		*	,	900
CG	יע <i>ב</i> י		AC.				r TC	C CA		C A		ATA			TAC		GT	r CT	T AC	ra r	T C	AC	AAA
GC	יי יי	AA C	TG	GTT	TCC	TT.	A AG	G GT	A CC	G T	TG	TAT	' AA	G	ATG	TÇ	A CAA	A GA	A TG	A T	A.C	TG	$\mathbf{T}\mathbf{T}\mathbf{T}$
Arg	g I	le A	sp	Gln	Ser	As:	n Se	r Hi	s A	la A	rsu	Ile	e Ph	ie '	Tyr	Ser	· Val	l Le	u Th	r II	.e Z	/sp	Lys>
			٥.	10			920				930				9	40			950	ł			960
		*		*		*	*		*		*		+			*		*	*			*	*
ΑT	G C	AG A	AC	AAA	GA	CAA	A GG	A CI	T T	AT A	ACT	TG	r co	T	GTA	. AG(G AG	r GG	A CC	Y A	CA	PTC	AAA
TA	C G	rc T	rtg	TTT	CT	G TT	T CC	T GA	A A	TA T	IGA	ACA	4 GC	CA C	CAT	TC	TC	A CC	T GO	T A	3T 2 >**	AAG Phe	TATT
Me	t G	ln A	lsn	Lys	As;	р Гу	's Gl	у ге	u T	yr :	mr	Cys	S AL	. <u>g</u>	val	. AL	3 36	T G1	.Y E.	.0 0	- <u>-</u> .		Lys>
			9	70			980)		9	990				10	00			1010)			1020
		*		*		*	+		*		*			*		*	~ ~~	*		k		*	*
TC	T G	TT A	AAC	AC(CTC	A GI	rg CI	AT A!	T AT	AT (GAT	'AA.	A.G.	CA om	CCC	יטט נ ממח ב	G GG	C GA	NG CK	CA CAT	фф WW	aga	TGT ACA
AG Se	ia c r v	AA al	l"IG Asn	ጥኩ ተ	s AG r Se	rr Va	al Hi	la I	le T	vr .	Asp	Ly	s A	la	Gl	, Pr	o Gl	у GI	lu P	ro L	ys	Ser	Cys>
	· - ·	· .			_ ,50					-	_	-											
			10	30			104				050			*		060		*	107			*	1080
~	\C ,	* 	y Cu		C 20			* ~		r TGC													GTC
C	rG n	dd	TGA	GT	G TO	T A	CG G	GT G	GC Z	ACG	GGI	r CG	T G	GΑ	CT	T GA	G G	C C	cc c	CT G	:GC	AGT	CAG
A:	sp I	ıγs	Thr	Hi	s Ti	ır C	ys P	ro P	ro () 'ys	Pro) Al	a F	ro	Gl	u Le	u Le	eu G	ly G	ly P	,LO	Ser	: Val>

Figure 16C

	1090				11	00			110		1120 * *			*	11	.30		1140		
TTC		TTC	* CCC	* CCA	AAA	* CCC .		* GAC	* ACC	CTC		ATC			ACC		GAG			
AAG	GAG	AAG	GGG	GGT	TTT	GGG	TTC	CTG	TGG	GAG	TAC	TAG	AGG	GCC	TGG	GGA	CTC	CAG	TGT	
Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr>	
		115	0		11	.60		1	.170			118	30		11	L90		1	200	
	*		*	*		*		*	*		*		*	*		*		*	*	
					GTG															
					CAC														Asp>	
Cys	Val	VAI	vai	Λου	vai	Der	1113	Giu	ىرىد	110	014	V CL _		2220	2 10 2 2		*3 ~	,	TADP.	
	*	121	LO *	*	12	220 *		*	L230 *		*	124	10 *	*	1250			*	1260 *	
GGC	GTG	GAG	GTG	CAT	AAT	GCC	AAG	ACA	AAG	CCG	CGG	GAG	GAG	CAG	TAC	AAC	AGC	ACG	TAC	
					ATT															
Gly	Va1	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr>	
	*	12	70 *	*	12	280		*	1290		*	130	00 *	*	1:	310		*	1320 *	
CGT	GTG	GTC	AGC	GTC	CTC	ACC	GTC	CTG	CAC	CAG	GAC	TGG	CTG	AAT	GGC	AAG	GAG	TAC	AAG	
					GAG															
Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	G1y	Lys	Glu	Tyr	Lys>	
		13	30		1	340			1350			13	60		1	370			1380	
	*		*	*		*		*	*		*		*	*		*		*	*	
																			AAA	
																			TTT Lys>	
Cys	пур	Val	561	TOIL	בענה	n,u	1100	110	nau	220		014	232	1111		DOI	2,2		270-	
	,	13	90 *			400 *		*	1410 *		*	14	20 *	*	_	430		*	1440	
GGG	* CAG	ccc		* GAA			GTG			CTG		CCA					CTG		AAG	
																			TTC	
Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Asp	Glu	Leu	Thr	. TAs>	
	*	14	50	*		.460		*	1470		*	14	.80 *	*		.490		*	1500	
AAC		GTYC	SAGC				CTC					TAT					: GCC		GAG	
																			CTC	
Asr	Glr	Val	. Ser	Leu	Thr	Cys	Leu	. Val	. Lys	Gly	Phe	Tyr	Pro	Ser	Asp) Ile	Ala	. Val	Glu>	
		1 =	510		1	.520			1530	,		15	40		1	.550			1560	
	*		*	*		*		*	*		*		*	*		*		*	*	
																			TCC	
																			AGG	
Tr	۱۲ی ر	ı ser	ASY	1 G13	/ GII	ı Pro	الك د	ı AST	ı Asr	ı TYI	т т	s Thi	. Thi	. Pro	Pro	va]	r ren	ASI	Ser>	
	*	15	570 *	,	*	L580 *		*	1590		*	1600		4	1610			*	1620 *	
																			G GGG	
																			C CCC	
Ası	o Gl	y Sea	r Phe	e Phe	e Lei	л Туг	: Sei	Lys	s Let	ı Th	r Va.	L ASI	э Буз	s Sei	: Arq	g 'Fri	o Gir	ı Gli	n Gly>	

Figure 16D

1690 1700

CTC TCC CTG TCT CCG GGT AAA TGA GAG AGG GAC AGA GGC CCA TTT ACT Leu Ser Leu Ser Pro Gly Lys ***>

Figure 17

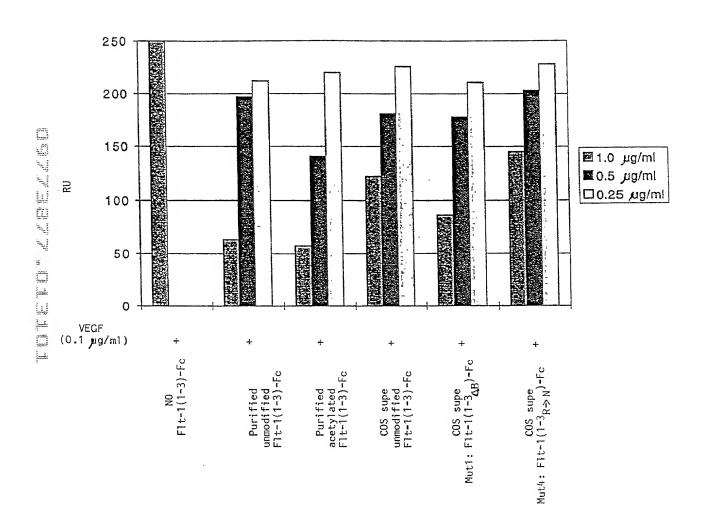


Figure 18

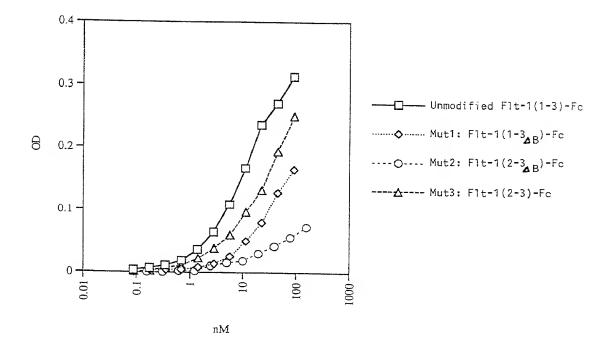
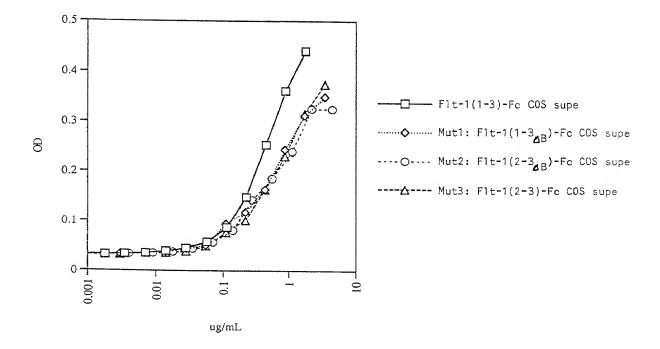
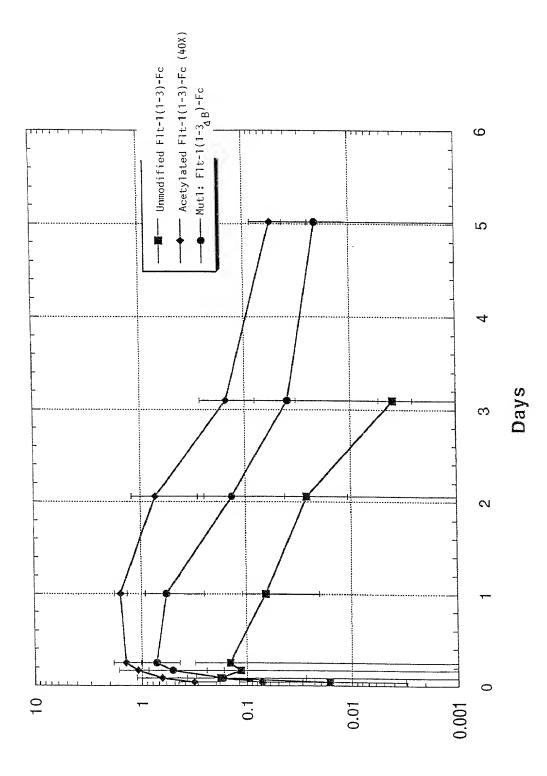


Figure 19







լա/6ո

Figure 21A

				>EcoR]	_site		
10	20	30	40	50	60	70	80
AAGCTTGGGCTGC							
PTCGAACCCGACG1	'CCAGCTAGC'I	GAGATCTCCI	AGCTAGGGG.	CCGCTCGAG	CTTAAGCGTTG		
						M V 1	S Y>
							>
					>BspEI_bric	dge	
8.0	100	110	100	120	1.0	150	1.50
rgggacaccgggg1							
ACCCTGTGGCCCC							
W D T G V	LLC	A L L	S C L I	LTG	S S>		
		FLT1 SS_			>		
					S	G>	
						> G R I) F V>
						G K 2	31
							>
170 AGAGATGTACAGTY	180			210		230	240
			HFLT1 D2				57
250	260	270	280	290	300	310	320
CTAACATCACTGT:							
SATTGTAGTGACA		TCAAAGGTGA	ACTGTGAAA	TAGGGACTAC	CTTTTGCGTA	TAGACCCTC	TCATCT
VTIN	T L K	KFPI	DTL	I P D	G K R I	I W D	S R>
			HFLT1 D2				84
330	340	350	360	370	380	390	400
AGGGCTTCATCAT							
FTCCCGAAGTAGT/ K G F T		_					
KGFI	SNA	түк	EIGI	LTC	E A T V	/ N G F	I L Y
			HFLT1 D2				1.
410	420	430	440	450	460	470	480
TAAGACAAACTAT							
ATTCTGTTTGATAC K T N Y	SAGTGTGTAGO L T H R				ACTCAGGCAGAC	STACCTTAAC	CTTGATA
T/ T T/ I		D2	т 1 Т	>			
				V V I	S P S	H G I	E L>
							137
					HFLK1 I	03	>

Figure 21B

amam		190	220		500				.0				~~~~						-			550			56	-
CTGT																										-
S V				L					T								G					W.				
																									1	64
				_							HFL	Kl.	D3_													>
									-		_															-
TCTI																										
AGAA S																										
5	5 1	× -	1 Q	П	. r.	K	. 1	ı V	. 1/	r	(L	, 1	N.		Τ	ي د	5 0	3 5	•]	Ľ,	M	K	K :			S>
											HFI.	ж1	D3													
																		-,-,-								
	(650			660			67	0		6	80			690)		70	0			710			72	0
CACC	TTA	ACTZ	TAG	ATG	GTG	TAA	.ccc	'GGA	GTG	ACC	CAAG	GAT	TGT	AC	ACC:	rgto	3CAC	CAT	CC.	AGT	GGG	CTG	ATG.	ACC.	AAC	A
GTGG	AAT:	rga:1	PATC	TAC	CAC	ATT	GGG	CCT	CAC	TGC	TTC	CTA	ACA!	TG'	IGG2	ACAC	GTC	GTA	\GG'	rca	CCC	GAC	TAC	TGG'	rtc	T
T	L	\mathbf{T}	I	D	G	V	T	R	S	D	Q	G	٦ :	Y	Т	С	A	A	S	S	G	L	Μ	T	K>	
																									21	
											_HFL	ıΚΙ	עצ											-		>
								> <	rf_	Bri	dae															
									·	1	.agc	_														
	,	730			740			75	0		7	60			770)		78	30			790			80	0
AGAA	CAG	CAC																								λA
	GTC								-																-	
												.ccs	C 1 G	тт.		7010	3101	ACC		199		933	100	100.	AC 1	
K N																										
			_EFL	ıvı	_בע					.> 	P	C۱														
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Figure 21C

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GCG(m	GA(3GG ⊃	CAC	SAC(CTG.	AGG	CTG(CGZ	AGG.	AAG?	AAGG	AGAI	ATC	GTTC K	GAG1	GGC:	ACCTY	GTTC	TCG:	rcc.	ACC	FTCG	TCC	JC
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Figure 22A

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90	100	110	120	130	140	150	160
TGGGACACCG(GGTCCTGCTG	TGCGCGCTGCT	CAGCTGTCTG	CTTCTCACAG	GATCTAGTTCC	GGAGGTAGACC	CTTTCGT
ACCCTGTGGC	CCAGGACGAC	ACGCGCGACGA	GTCGACAGAC	GAAGAGTGTC	CTAGATCAAGG	CCTCCATCTGC	BAAAGCA
WDTC	3 V L L	CALI	SCL	L L T	G S S>		
	FL	T1 SIGNAL S	EQUENCE		>		
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170	180	190	200	210	220	230	240
					CTCGTCATTCC		
					CICGICATICC GAGCAGTAAGG		
E M Y	S E I P		H M T E		L V I P		T S>
11 11 1	0 1 1 1				_ v _ i	C 11 V	57
		I	TLT1 IG DOM	IAIN 2			>
250	260	270	280	290	300	310	320
CTAACATCAC	TGTTACTTTAA	AAAAGTTTCC	ACTTGACACTT	TGATCCCTGA	TGGAAAACGCA	TAATCTGGGA	CAGTAGA
GATIGTAGIG.	ACAATGAAATT	TTTTCAAAGG:	rgaactgtgaa	ACTAGGGACT	ACCTTTTGCGT	'ATTAGACCCT	GTCATCT
P N I T	V T L	K K F P	L D T	LIPD	G K R	I I W D	S R>
							84
			FLT1 IG DOM	MAIN 2			>
330		350	360		380	390	400
					GTGAAGCAACA		
					CACTTCGTTGT		
KGF	IISN	АТУІ	K E I G	L L T	CEAT	A 10 G	H L Y> 11
			armi ro por	57 TNT O			T 1
			FLT1 IG DON	IALN Z			
410	420	430	440	450	460	470	480
					TGTTGCCCAG		
					GACAACGGGTC		
		AGCIGITIGG					
		DOMAIN 2_					
					LLPR	K S L	E L>
				~			137
				VE	GFR3 (FLT4)	IG DOMAIN	3

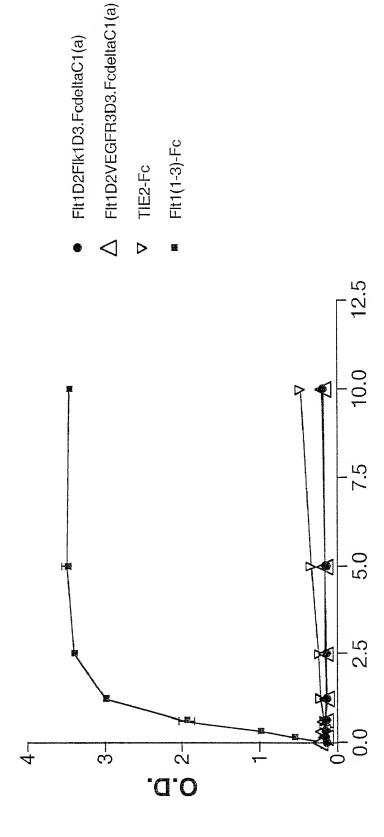
Figure 22B

		90			500			51				520			530			54				50			560
TGGTA ACCAI																									
accai L V		E			V.	L L	N	C							N			V				W			
								VE	GFR	.3	(FL	T4)	IG	DO:	NIAN	3									>
		570			580			59	-			600			610			62				530			640
GGGA/																									
G I					(G										Q Ç		H			C I					T> 191
								VE	EGFF	13	(FL	T4)	IG	DO	NIAM	1 3_									>
		650			660			67				680			690				0			710			720
CATC																									
I		N				H			G	S					A			G		Q		F		E	S> 217
								VI	EGFI	3	(FI	T4)	IG	DC	ILAM	v 3_									>
		730			740)		75	50			760)		77()		78	30			790			800
CCGA	GGT	CAT	TGT		rga <i>z</i>	AAA		ccc	GG(CGA	CAF	AAA	TCA	.CAC	ATG	CCC	ACC(GTGC							
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															-										
GGAC		810 CAC		TCC	82 TCT			8 CAA							85 'TGA			86 EGA		CTG	AGG	870 ACT:		GCG	880 TGGT
	GCA	GTC		AGG	AGA	AGC	GGG	GTT	TTG	GG1	rrc(CTG:	rggc	GAG"	PACT.	AGA	GGG	CTY	GG(GAC	TCC	AGI	GTA	CGC	ACCA V V> 27:
									F	СΔ	C1	- A	AL	COT	YPE_										>
GGTG	GAC	890 GTG		'CAC	90 GAA		cci) CTGK				GGC		40 GAG					'AAG	960 ACAA
CCAC	CTC		TCG		CTT			YCTC	CAG	TT	CAA	GTT	GAC	TAC		CTG	CCG	CAC	CTC	CAC	GTA	TTT		TTC	TSTT T> 297
									F	CΔ	C1	- A	AL.	LOT	YPE_										>
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TCG	GCG(CCC.	rcci	CG1	CAT	GT.	rgTo	CGTC	CAT	GG	CAC	ACC.	AGT	CGC.	AGGA	GTG	GCA	GGA	CGT	GGT	CC.	rga(CCGA	7CZJ	ATGGC PACCG 1 G>
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									F	$C\Delta$	C1	- A	. AL	LOT	YPE_										^

Figure 22C

1050	1060 1070	1080	1090	1100	1110	1120
	CAAGGTCTCCAACAAAGCC					
	GTTCCAGAGGTTGTTTCGGC					
KEYKC	K V S N K A	LPAE	PIEK	TIS	K A K G	Q P> 351
	FCΔ(C1 - A ALLO	TYPE			>
		>7	x>C_A_allo 	type		
		>G>T_A	_allotype			
1130	1140 1150	1160	11170	1180	1190	1200
	TGTACACCCTGCCCCCATC	CGGGATGAG	TGACCAAGA	ACCAGGTCAGC	CTGACCTGCC	TGGTCA
GGCTCTTGGTGTCC	ACATGTGGGACGGGGTAG	GCCCTACTCC	GACTGGTTCT	TGGTCCAGTCG	GACTGGACGC	ACCAGT
REPQ	V Y T L P P S	RDE	L T K	n Q v s	L T C	L V>
						377
	FCΔ(C1 - A ALLO	TYPE			>
1210	1220 1230	1240	1250	1260	1270	1280
AAGGCTTCTATCCC	AGCGACATCGCCGTGGAGT	GGGAGAGCAA	rgggcagccg	GAGAACAACTA	LCAAGACCACG	CCTCCC
	FC∆	C1 - A ALLO	OTYPE			404
		>T>C				
	1010	1222			4256	1260
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	.CGGCTCCTTCTTCCTCTAT. 'GCCGAGGAAGAAGGAGATA'					
	GCCGAGGAAGAAGAAAA) G S F F L Y			CICGICCACCO		
V B D S 1	, 6 3 1 1 1 1			. 5 1. W	2 2 3 1	43
	FCV	C1 - A ALLO	TYPE			>
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1370	1380 1390	1400	1410	1420	1430	1440
CTCATGCTCCGTG	ATGCATGAGGCTCTGCACAA	CCACTACACG	CAGAAGAGCC	TCTCCCTGTCT	CCGGGTAAA	rgagcgg
GAGTACGAGGCAC	ACGTACTCCGAGACGTGTT	GGTGATGTGC	GTCTTCTCGG	AGAGGGACAGA	GGCCCATTT!	ACTCGCC
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					455	5
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CCGC						
CCCC						

Figure 23



[Modified FIt receptor] (nM)

41/65 Figure 24A

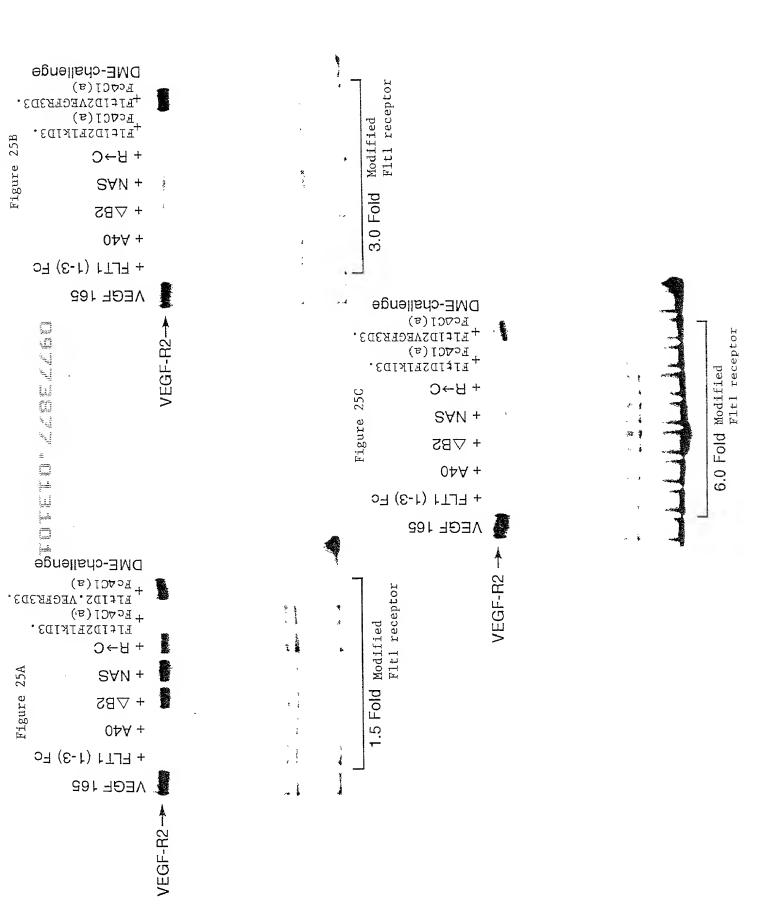
10	20	30	*	40 *	50 *	60
TAC CAG TCG ATG	ACC CTG TGG W D T		C GAC ACG L C	CGC GAC GAG A L L		
70 *	83 *	90		100	110	120
ACA GGA TCT AGT TGT CCT AGA TCA . T G S S	AGG CCT TCA S G>					
21_hFLT1 SIGNAL	SEQ_26> S _27_	D T G		F V E G DOMAIN 2_	M Y S	E I> 40>
130	140	150	0	160 *	170 *	180 *
CCC GAA ATT ATA GGG CTT TAA TAT P E I I 41		CTT CCT TCC E G R	C CTC GAG	CAG TAA GGG V I P		
190 *	200	210	0	220	230	240
CCT AAC ATC ACT GGA TTG TAG TGA P N I T 61	GTT ACT TTA	AAA AAG TIT TIT TIC AAA K K F	T CCA CIT A GGT GAA	CTG TGA AAC D T L	TAG GGA CTA	
250	260	270	′0 *	280	290	300
CGC ATA ATC TGG GCG TAT TAG ACC R I I W 81	GAC AGT AGA	AAG GGC TIX TIC CCG AAG K G F	C ATC ATA G TAG TAT	TCA AAT GCA AGT TTA CGT S N A	ACG TAC AAA TGC ATG TTT T Y K	
310	320 *	33	50 *	340	350	360 *
GGG CTT CTG ACC CCC GAA GAC TGG G L L T	TGT GAA GCA ACA CTT CGT C E A	ACA GTC AA	AT GGG CAT PA CCC GTA 1 G H	AAC ATA TIC	TGT TIG AT	
370 *	380	39		400	410 *	420 *
CAT CGA CAA ACC GTA GCT GTT TGG H R Q T 121hFLT1:	AAT ACA ATC TTA TGT TAG N T I	ATA GAT GT TAT CTA CA I D>	G GTT CIG	AGT CCG TCT	CAT GGA AT	r gaa cta
121 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	10 WIWIN 2_	V		S P S _hFLK1 IG DO		

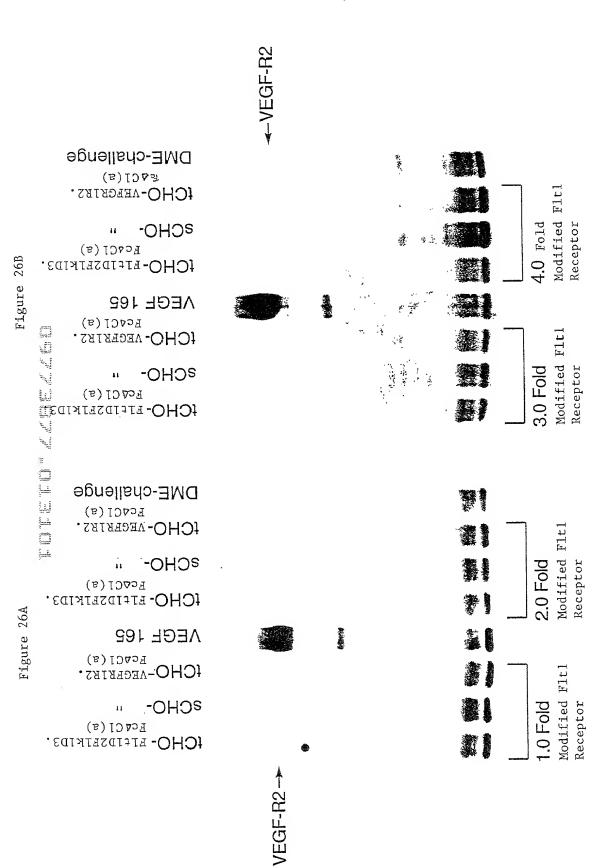
42/65 Figure 24B

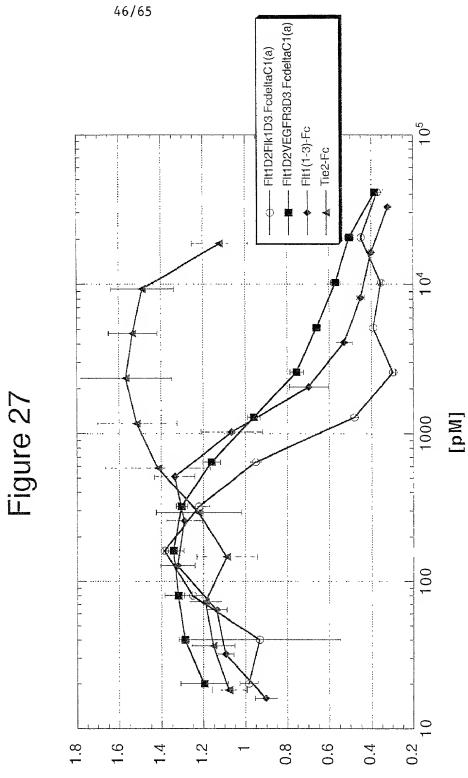
430	440	450	46		470 *	480 *
TCT GTT GGA GAA AGA CAA CCT CTT S V G E 141	AAG CTT GTC TTC GAA CAG K L V	TTA AAT TGT AAT TTA ACA L N C	ACA GCA AGA . TGT CGT TCT T A R	ACT GAA CTA TGA CTT GAT T E L	AAT GIG GGG TTA CAC CCC N V G	ATT TAA I>
490 ×	500 *	510 *	52	* *	530	540 *
GAC TTC AAC TGG CTG AAG TTG ACC D F N W 161	CTT ATG GGA E Y P	AGA AGC TTC S S K	GTA GTC GTA H Q H	TTC TTT GAA K K L	CAT TIG GCT V N R	CTG D>
550	560 *	570 *		30 *	590 *	600
CTA AAA ACC CAG GAT TTT TGG GTC L K T Q 181	TCT GGG AGT AGA CCC TCA S G S	GAG ATG AAG CTC TAC TTC E M K	AAA TTT TTG TTT AAA AAC K F L	AGC ACC TTA TCG TGG AAT S T L	ACT ATA GAT TGA TAT CTA T I D	CCA G>
610	620 *	630 *	64			660
GTA ACC CGG AGT CAT TGG GCC TCA V T R S 201	GAC CAA GGA CTG GTT CCT D Q G	TIG TAC ACC AAC ATG TGG L Y T	TGT GCA GCA ACA CGT CGT C A A	TCC AGT GGG AGG TCA CCC S S G	CTG ATG ACC GAC TAC TGG L M T	TTC K>
670 *	680 *	690 *	70	00	710	720 *
AAG AAC AGC ACA TTC TTG TCG TGT K N S T 221hFL	TTT GTC AGG AAA CAG TCC F V R	GTC CAT GAA CAG GTA CTT V H E	AAG GAC AAA TIC CIG TIT K>	ACT CAC ACA	TGC CCA CCG	TGC
			D K		C P P	
730	740	750 *	76	50	770	780 *
CCA GCA CCT GAA GGT CGT GGA CTT P A P E 241	. CTC CTG GGG 'GAG GAC CCC L L G	GGA CCG TCA CCT GGC AGT G P S	GTC TTC CTC	TTC CCC CCA AAG GGG GGT F P P	AAA CCC AAG TTT GGG TTC	GAC CTG D>
790 *	800	810		20	830	840 *
ACC CTC ATG ATC TGG GAG TAC TAG T L M I 261	AGG GCC TGG S R T	GGA CTC CAG P E V	TGT ACG CAC T C V	CAC CAC CTC	CAC TCG GTC V S H	CTT E>
850 *	860 *	870 *	88	80 *	890	900
GAC CCT GAG GTC CTG GGA CTC CAG D P E V 281	TTC AAG TTG K F N	TGG TAC GTG ACC ATG CAC W Y V	GAC GGC GTG CTG CCG CAC D G V	GAG GTG CAT CTC CAC GTM E V H	T AAT GCC AAK A TTA CGG TIK N A K	T>

Figure 24C

	91	LO		9	20			930				.0 *		Š	950			960
AAG CCC TTC GGC K P 301	GCC R	CTC E	CTC E	CAG GIC Q	TAC ATG Y	TIG N	TCG S	ACG TGC T	ATG Y	GCA R	GTG CAC V	GTC CAG V	TCG S	CAG V	GAG L	TGG T	CAG V	GAC L>
	97	'0 *		9				990			100				10		1	020
CAC CAC GTG GTC H Q 321	CTG D	ACC W	GAC L	TTA N	CCG G	AAG TTC K	GAG CTC E	TAC ATG Y	AAG TTC K	TGC ACG C	AAG TTC K	GTC CAG V	AGG S	TTG N	TTT K	CGG A	GAG L	GGT P>
	10	30		10			=	1050			106	50 *		10	070 *		:	L080 *
GCC CCC CGG GGC A P 341	TAG I	CTC E	TTT K	TGG T	TAG I	AGG S	AAA TTT K	GCC CGG A	AAA TTT K	GGG GGG	CAG GTC Q	CCC GGG P	CGA GCT R	GAA CTT E	CCA GGT P	CAG GTC Q	GTG CAC V	TAC ATG Y>
	10	90 *		13	L00 *		:	1110			112	20		1	130			1140
ACC CT TGG GA T L 361	GCC GGG P	CCA GGT P	TCC AGG S	CGG GCC R	GAT CTA D	GAG CTC E	CTG GAC L	ACC TGG T	AAG TTC K	AAC TTG N	CAG GTC Q	GTC CAG V	AGC TCG S	CTG GAC L	ACC TGG T	TGC ACG C	CTG GAC L	GTC CAG V>
	11	50 *		1:	160 *		:	1170 *			11:	80 *		1	190			1200 *
AAA GG	TIC			AGC														
K G 381	F	ATA Y	P	S	D	I	Α	V	CTC E	ACC W	CTC E	TCG S	TTA N	CCC G	GTC Q	GGC P	CTC	TTG N>
K G	F	Y Y	P _385.	S	D	I	A h	V FCACI	CIC E L A _	ACC W	CIC	TCG S	TTA N _395_	G G	GTC Q	GGC P	E	TTG N>
K G	F 12 C AAG G TTC K	Y 10 * ACC TGG	P _385 ACG TGC T	S 1: CCT GGA P	D 220 * CCC GGG P	I GTG CAC V	A h	V FCACI 1230 * GAC CTG D	CTC E A TCC AGG S	ACC W GAC CTG D	CTC E 12 GGC CCG G	TCG S 40 * TCC AGG S	TTA N _395_ TTC AAG F	CCC G 1 TTC AAG F	GTC Q 250 * CTC GAG L	GGC P TAC ATG	E AGC	TTG N>_400> 1260 * AAG TTC K>
K G 381 AAC TA TTG AT N Y	F 12 C AAG G TIC K	Y 10 * ACC TGG	P _385 ACG TGC T	S 1: CCT GGA P	D 220 * CCC GGG P	I GTG CAC V	A h	V FCACI 1230 * GAC CTG D	CTC E LA_ TCC AGG S LA_	ACC W GAC CTG D	CTC E 12- GGC CCG G	TCG S 40 * TCC AGG S	TTA N _395_ TTC AAG F	CCC G 1 TTC AAG F	GTC Q 250 * CTC GAG L	GGC P TAC ATG	E AGC	TTG N>_400> 1260 * AAG TTC K>
K G 381 AAC TA TTG AT N Y	F 12 C AAG G TIC K 12 C GIC G CAC	ATA Y 10 * ACC TGG T 270 * GAC CTG	P _385 ACG TGC T _405 AAG	S 1: CCT GGA P 1 AGC TCG S	D 220 * CCC GGG P 280 * AGG TCC R	GTG CAC V TGG ACC	A h	V FCAC: 1230 * GAC CTG D FCAC: 1290 * CAG GTC Q	TCC AGG S A A CCC G	ACC W GAC CTG D AAC TTG	CTC E 12. GGC CCG G 13 GTC CAG V	TCG S 40 * TCC AGG S 00 * TTC AAG F	TTA N 395 TTC AAG F 415 TCA AGT S	CCC G 1 TTC AAG F 1 TGC ACG C	GTC Q 250 * CTC GAG L 310 * TCC AGG s	GGC P TAC ATG Y GTG CAC V	AGC TCC S	TTG N> _400> 1260
K G 381 AAC TA TTG AT N Y 401 CTC AC GAG TG	F 12 C AAGG TTO K 12 C GTG G CAC V	ATA Y 10 * ACC TGG T 270 * GAC CTG	P _385 ACG TGC T _405 AAG TTC K _425	S 1: CCT GGA P 1 AGC TCG S	D 220 * CCC GGG P 280 * AGG TCC R	GTG CAC V TGG ACC	A h	V FCAC: 1230 * GAC CTG D FCAC: 1290 * CAG GTC Q FCAC:	TCC AGG S I A CCC G G I A C	ACC W GAC CTG D AAC TTG	CTC E 12. GGC CCG G 13 GTC CAG V	TCG S 40 * TCC AGG S 00 * TTC AAGG F	TTA N 395_ TTC AAG F 415_ TCA AGT S 435_	CCC G 1 TTCC AAG F 1 TGCC ACG C	GTC Q 250 * CTC GAG L 310 * TCC AGG S	GGC P TAC ATG Y GTG CAC V	AGC TCC S	TTG N> _400> 1260 * AAG TTC K> _420> 1320 * CAT GTA H>







Absorbance 450/570nm

Figure 28

Bine	Binding Stoichiometry of hVEGF	hiometry of hVEGF165 to F1t1D2F1k1D3.FcdC1(a) & VEGFR1R2-Fc4C1(a)
hVEGF165 (nM)	VEGF/Flt1D2F1k1D3.FcAC1(a)	VEGF/VEGFR1R2-Fc4C1(a)
	0.93	0.98
10	76.0	0.94
50	1	0.99
Average±StDev	0.96±0.03	0.97±0.02

Figure 29

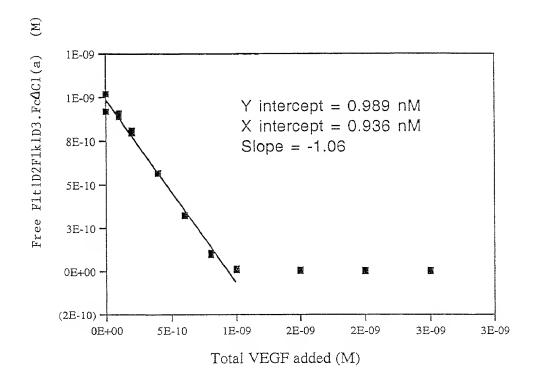


Figure 30

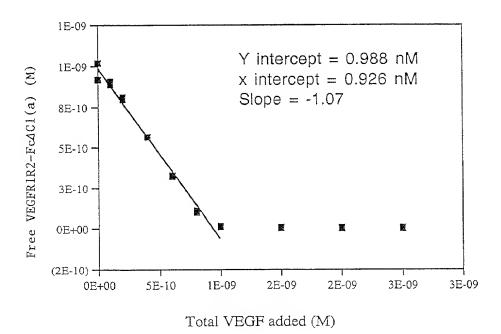


Figure 31

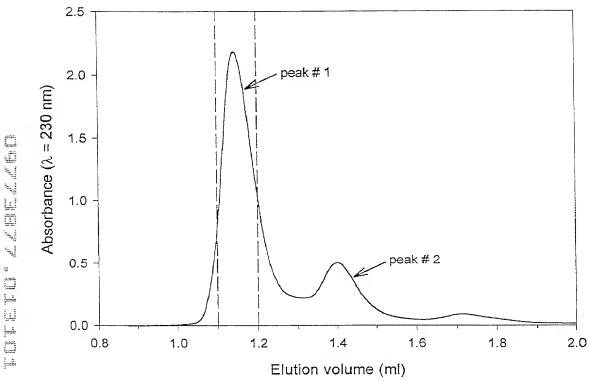


Figure 32

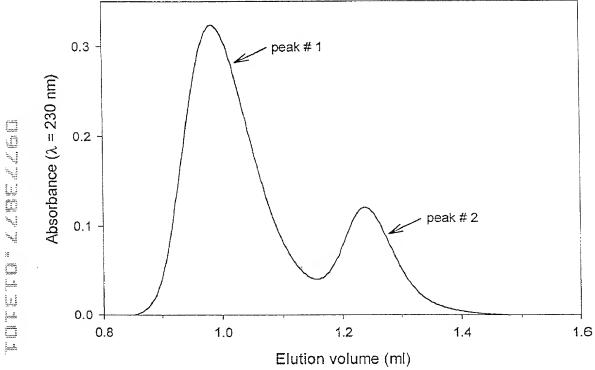


Figure 33

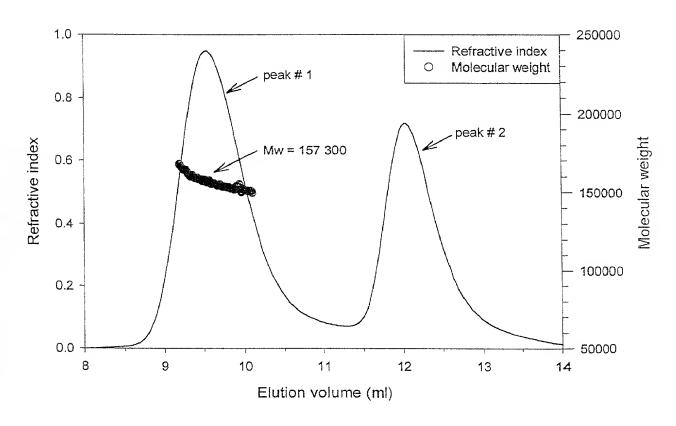


Figure 34

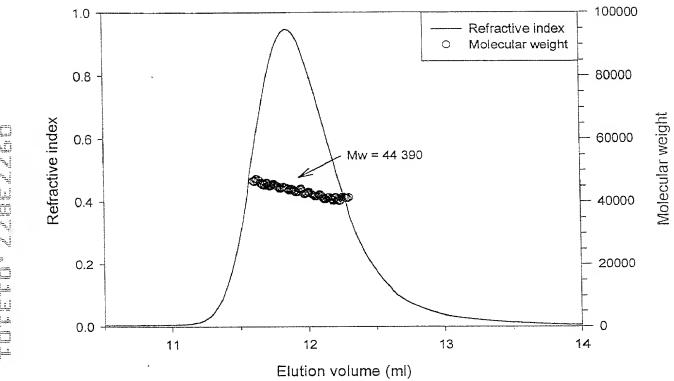


Figure 35

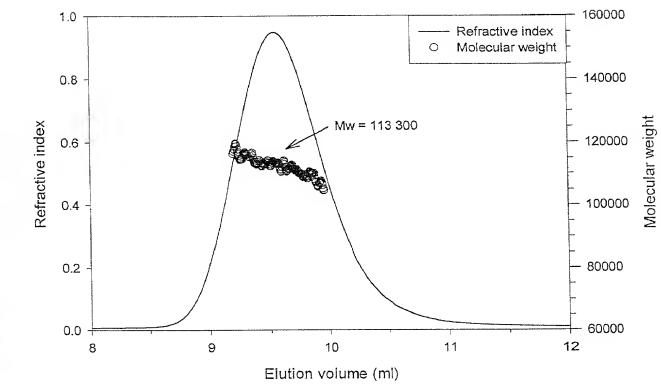


Figure 36

350 GKEYK<u>C</u>KVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL DLKTQSGSEMKKFLSTLTIDGVTRSDQGLYT<u>C</u>AASSGLMTKK<u>N</u>STFVRVH VVLSPSHGIELSVGEKLVL<u>NC</u>TARTELNVGIDFNWEYPSSKHQHKKLVNR TCL VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL YSKLTVDKS KRIIWDSRKGFIIS<u>N</u>ATYKEIGLLT<u>C</u>EATVNGHLYKTNYLTHRQTNTIID GRPFVEMYSEIPEIIHMTEGREL VIPCRVTSP<u>N</u>ITVTLKKFPLDTLIPDG RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 37

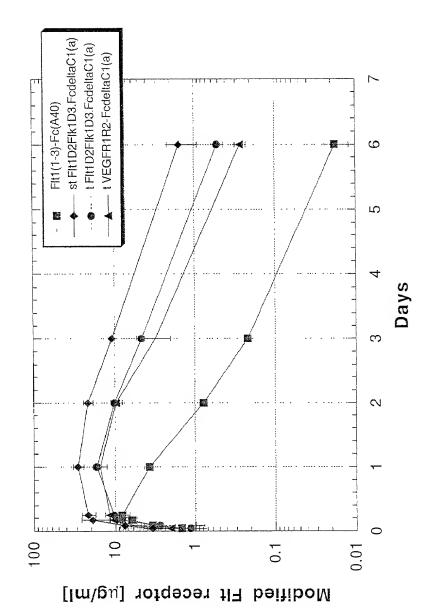
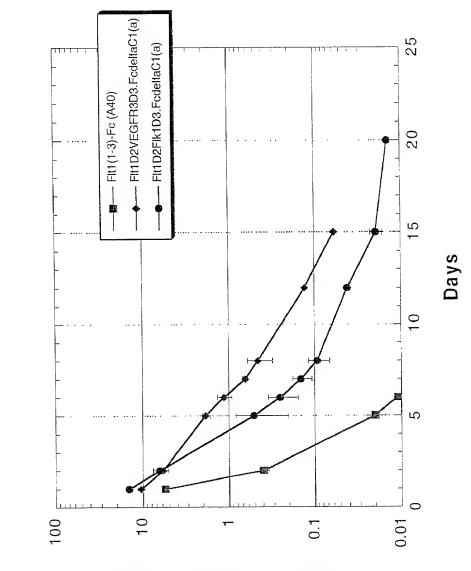


Figure 38



Modified Fit receptor [µg/ml]

Figure 39

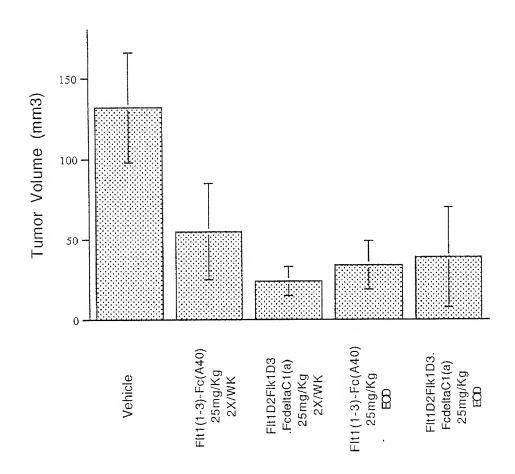


Figure 40

